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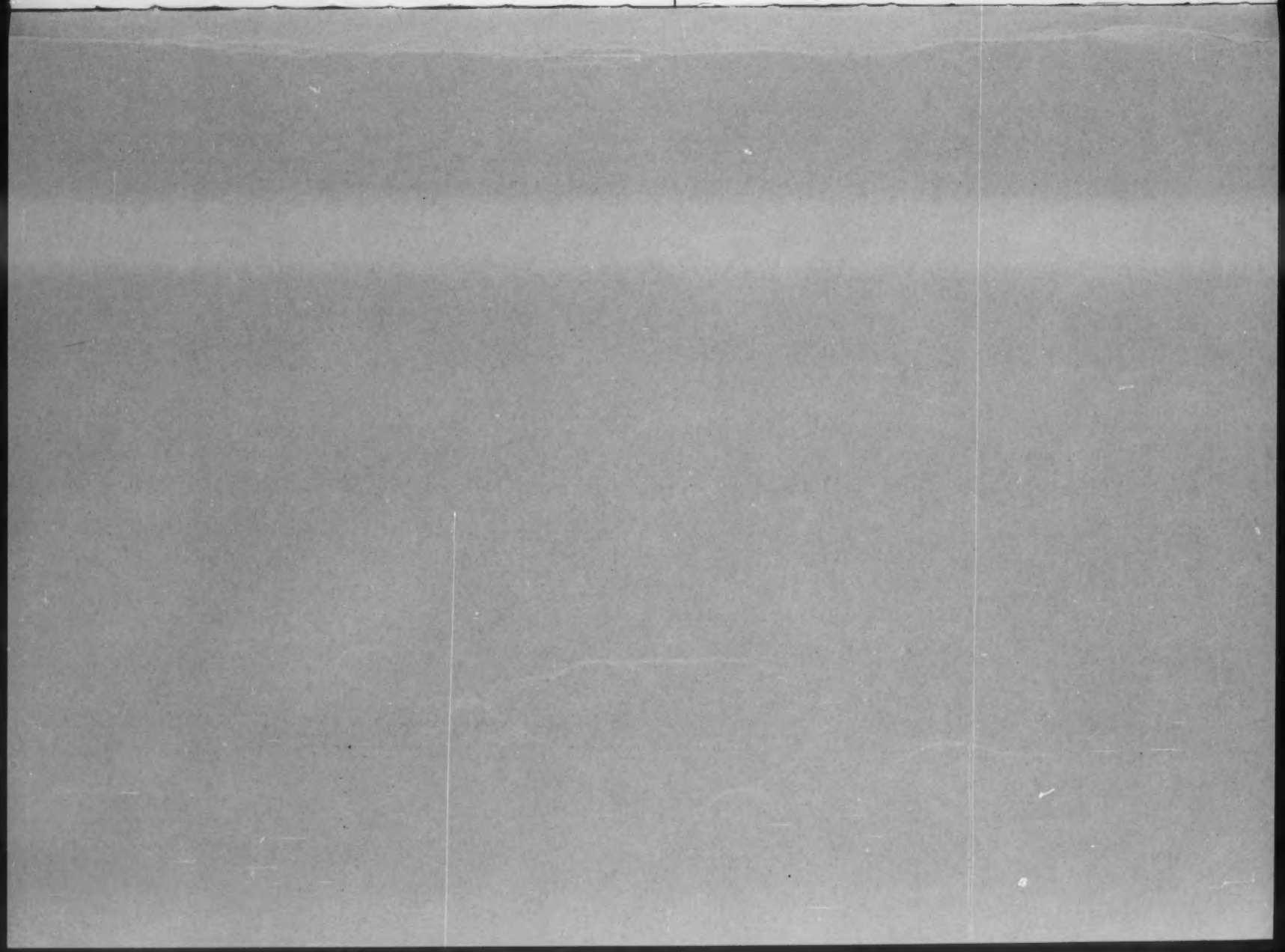
BULLETIN ON

NARCOTICS

Vol. XI, No. 3, JULY-SEPTEMBER 1959

UNITED NATIONS



Bulletin on NARCOTICS

Vol. XI, No. 3, JULY-SEPTEMBER 1959

UNITED NATIONS

DIVISION OF NARCOTIC DRUGS

Geneva

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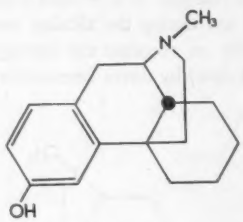
Some recent advances in the chemistry of the opium alkaloids

By David Ginsburg
Department of Chemistry, Israel Institute of Technology, Haifa, Israel

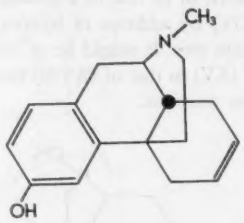
The last review article in this series covered work published in the chemical literature through most of 1957 (1). The papers reviewed in the present article may be divided into several types : (*a*) Synthetic analgesics structurally related to the morphine alkaloids; (*b*) Interrelationships among various morphine derivatives; (*c*) A continuation of the structural elucidation of Diels-Alder adducts of thebaine.

I. Synthetic Studies directed towards the Preparation of Analgesic Compounds

An extremely interesting account has been published by Gates & Webb (2) describing the synthesis of 3-hydroxy-N-methyl-*iso*morphinan (I) and of 3-hydroxy-Δ^6-dehydro-N-methyl-*iso*morphinan (II).



I



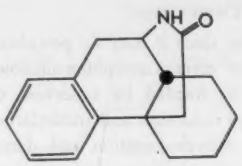
II

Both of these synthetic substances were resolved, and the *l*-isomer of each was shown to possess powerful analgesic activity. *l*-3-Hydroxy-N-methyl-*iso*morphinan (I) is 8 to 10 times as active as morphine as determined by the D'Amour-Smith tail-flick method, whilst the *l*-isomer of (II) is only slightly less active.

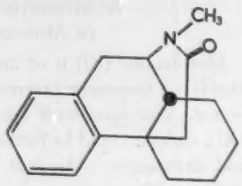
The synthesis of these compounds extends the method developed by Gates in his total synthesis of morphine, thus increasing the number of valuable products which may be obtained by the first successful synthetic approach to this complex natural product. Here also a naphthaquinone derivative reacted with butadiene and afforded rings A, B, and C of the morphine skeleton. Subsequent cyclization of the lactam ring afforded the tetracyclic skeleton of the alkaloid.

The resolution of the synthetic compounds (I) and (II) was effected with the enantiomorphic dibenzoyltartaric acids. Because of synthetic difficulties, (II) was obtained via the O-methyl ether, which was later cleaved by potassium hydroxide to afford the corresponding phenol.

3-Hydroxy-N-methyl-*iso*morphinan (I) could also be obtained by nitration of the lactam, 16-oxo-N-methyl-*iso*morphinan (IV) which, in turn, was obtained by methylation of 16-oxo-*iso*morphinan (III) with methyl iodide in the presence of sodium hydride.

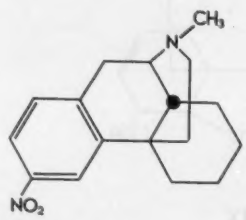


III



IV

Nitration of (IV) gave a mixture, containing preponderantly the 3-nitro-isomer (V), which was accompanied by lesser amounts of the 1- and 2-nitro derivatives. All three isomers were separated and each was converted in a series of steps into the corresponding (1-, 2-, and 3-) amino derivatives. Diazotization and hydrolysis converted each amine of type (VI) to the corresponding phenol (I and 1- and 2-hydroxylic isomer).



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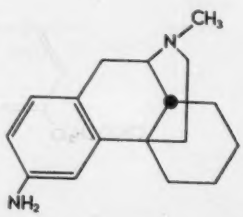
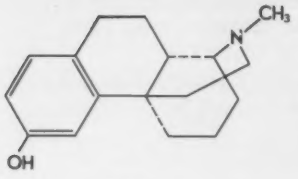


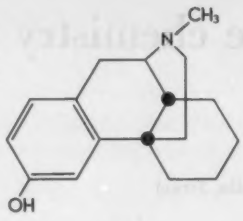
VI

The structural assignments for the minor isomers were made on the basis of infrared analogies to suitably substituted benzene derivatives and attack (by nitration) of the 4-position was reasonably ruled out on the basis of both steric and electronic considerations.

Although a new compound (VII) prepared by May (3) does not possess the skeletal structure of morphine, it is felt that it falls within the scope of this review for two reasons. It was prepared in order to determine whether it would possess analgesic activity and it is a positional isomer of 3-hydroxy-N-methyl-morphinan (VIII).



VII



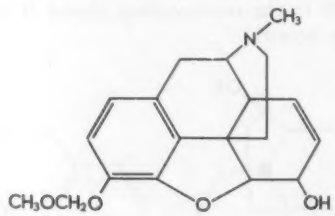
VIII

The new compound, 1,2,3,9,10,10a-hexahydro-6-hydroxy-11-methyl-1,4a (4H)-iminoethanophenanthrene (VII) had less than 2% of the analgesic potency of racemic 3-hydroxy-N-methyl-morphinan (VIII).

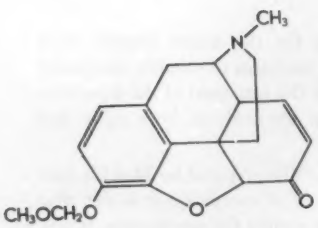
II. Synthetic Interconversions of Morphine Derivatives

Morphinone (XI) is of interest, since it may be postulated that it is a biogenetic precursor of certain morphine alkaloids — e.g., morphine itself could be formed by reduction of (XI), codeine could be formed by reduction and methylation and thebaine would result by dehydrogenation and dimethylation (4).

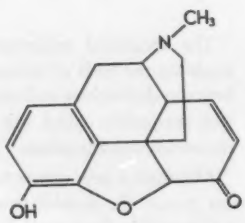
Rapoport and his co-workers (5) have recently prepared this sensitive ketone (XI) by oxidation of morphine whose phenolic group was protected with a methoxymethyl group (IX), by means of silver carbonate in benzene. The protecting group still present in (X) could be removed under mild acidic conditions or on a sulfonic acid type ion exchange resin. Elution from the resin must be carried out under very-well-defined conditions in order to avoid the destruction of (XI) by alkali towards which it is extremely sensitive.



IX



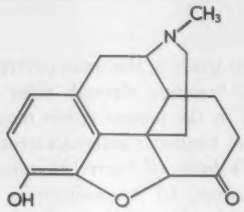
X



XI

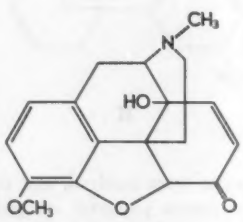
Reduction of morphinone with sodium borohydride was possible and gave morphine. Its reduction with 5% palladized carbon in ethanol gave dihydro-morphinone (XII).

Treatment of (X) with methyl lithium followed by hydrolysis of the methoxymethyl protecting group gave 6-methylmorphine which upon methylation could be converted into 6-methylcodeine.

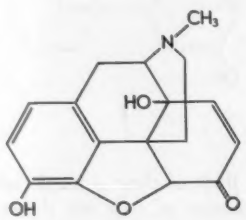


XII

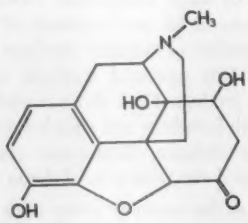
Weiss (6) has shown that 14-hydroxycodeine (XIII) can be demethylated with aqueous hydrobromic acid to afford 14-hydroxymorphinone (XIV). (No skeletal rearrangement occurs, since the 14-position is blocked.) (XV) was shown to accompany (XIV) as a reaction product, but the co-appearance of 8,14-dihydroxydihydromorphinone (XV) was shown to be due to a secondary reaction. It is formed from (XIV) by addition of hydroxyl ion during the alkaline isolation step. It would be of interest to correlate the stucture of (XV) to that of (XVIII) (see below) by direct interconversion reactions.



XIII



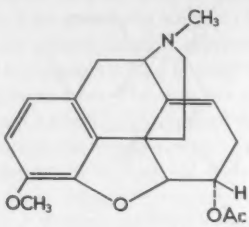
XIV



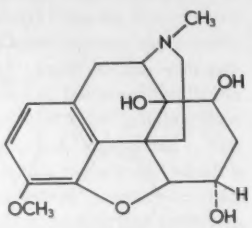
XV

Sargent, Schwartzman & Small (7) have reported the preparation of a series of hydroxylated codeine and neopine derivatives by treatment with osmium tetroxide and decomposition of the osmate esters. Although the hope that these products might be pharmacologically active was not realized, several steric conclusions were drawn from this work.

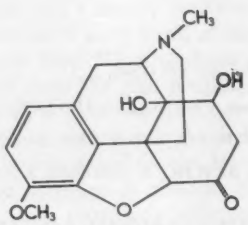
For example, osmium tetroxide hydroxylation of acetylneopine (XVI) gave a presumed *cis*-glycol (XVII). Vieböck (8) had previously obtained 8,14-dihydroxydihydrocodeinone (XVIII) by oxidation of thebaine with manganic acetate followed by treatment with hot dilute hydrochloric acid.



XVI



XVII



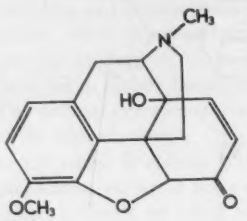
XVIII

Reduction of Vieböck's ketone (XVIII) with lithium aluminium hydride or with sodium borohydride gave a mixture of epimeric (at C_6) 8,14-dihydroxydihydrocodeines. One of these was identical with (XVII), proving that the 8- and 14-hydroxyl groups are disposed in the *cis*-fashion. In the other epimer, the authors assume that the apposite configuration of the hydroxyl obtains at C_6.

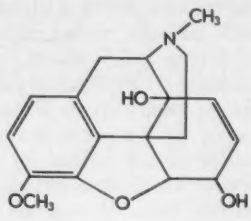
14-Hydroxycodeine (XX) was prepared by sodium borohydride reduction of 14-hydroxycodeinone (XIX). By analogy to the stereospecific reduction of codeinone to codeine by means of this reducing agent (9), the authors infer that (XX) has the codeine configuration of the hydroxyl group at C_6 and that its reduction product, 14-hydroxydihydrocodeine-B has the similar configuration at C_6. The C_6-epimer of the latter, 14-hydroxydihydrocodeine-C is therefore assumed to have the *iso*codeine configuration. It is a pity that the authors have not proved this point conclusively by studying the rates of hydrolysis — e.g., of the acetates of the pair of epimers 14-hydroxydihydrocodeine-B and -C (cf. 10).

Rapoport and co-workers (11) have shown that aldehyde degradation products of codeine very readily lose carbon monoxide to give a benzofuran derivative — e.g., 6,7,8,9,10, 14-hexahydromorphenol methyl ether.

Codeine was converted via its tosylate to Δ^7-desoxycodeine through treatment of the tosylate with lithium aluminum hydride. Degradation to the methine and to the 13-vinyl derivative (XXI) was effected in 52% over-all yield from codeine, since there was no hydroxyl group at C_8 to lower the yield through interaction during the Hofmann degradation steps. The vinyl compound was quantitatively hydroxylated by means of osmium tetroxide, and the resulting glycol (XXII) was cleaved to the aldehyde (XXIII) by means of sodium periodate. The aldehyde was very readily decarbonylated through a free radical mechanism under a variety of reaction conditions to yield the substituted benzofuran (XXIV).



XIX



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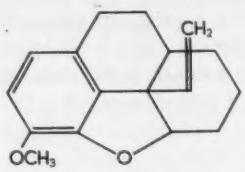
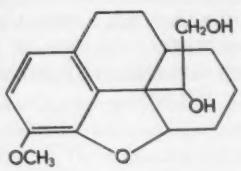
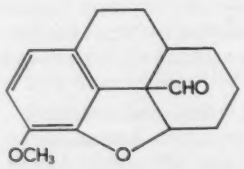


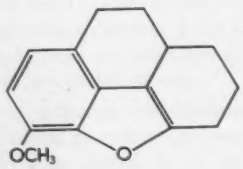
XXI



XXII



XXIII



XXIV

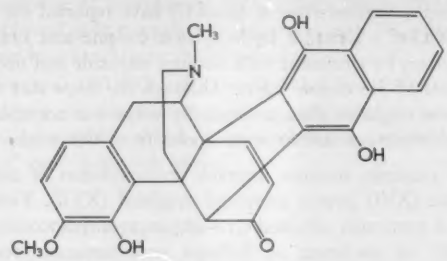
III. Thebaine Adduct with 1,4-naphtaquinone

Bentley, Ball & Cardwell (12) have published an additional paper in the field of Diels-Alder adducts of thebaine. The

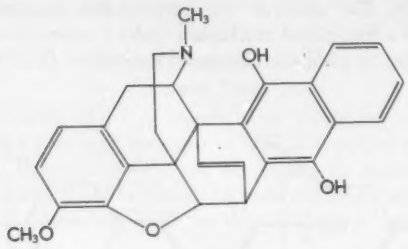
1,4-naphthaquinone adduct of thebaine has been shown to parallel in its chemical behaviour that of the analogous benzoquinone adduct.

The naphthaquinone adduct is unstable, and cannot be isolated as such. It was readily isomerized to thebaine-1,4-naphthaquinol (XXV).

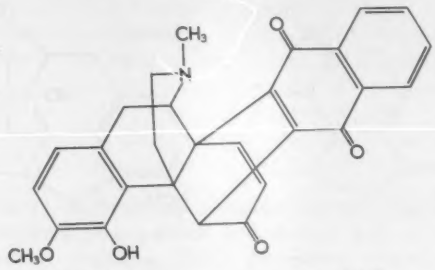
The acid rearrangement product, benzflavothebaone (XXVI), is analogous to flavothebaone, but in contradistinction to the latter it is very readily oxidized by air in alkaline solution to the quinone (XXVII).



XXVI



XXV



XXVII

References

(1) GINSBURG, *Bulletin on Narcotics*, Vol. X, No. 2, 1 (1958).

(2) GATES & WEBB, *J. Amer. Chem. Soc.*, *80*, 1186 (1958).

(3) MAY, *J. Org. Chem.*, *23*, 947 (1958).

(4) *Cf.* SCHÖPF, *Naturwiss.*, *39*, 241 (1952).

(5) RAPOPORT, BAKER & REIST, *J. Org. Chem.*, *22*, 1489 (1957).

(6) WEISS, *J. Org. Chem.*, *22*, 1505 (1957).

(7) SARGENT, SCHWARTZMAN & SMALL, *J. Org. Chem.*, *23*, 1247 (1958).

(8) VIEBÖCK, *Ber.*, *67*, 197 (1934).

(9) GATES, *J. Amer. Chem. Soc.*, *75*, 4340 (1953).

(10) ELAD & GINSBURG, *J. Amer. Chem. Soc.*, *78*, 3691 (1956).

(11) RAPOPORT, BATCHO & GORDON, *J. Amer. Chem. Soc.*, *80*, 5767 (1958).

(12) BENTLEY, BALL & CARDWELL, *J. Org. Chem.*, *23*, 941 (1958)

Some remarks on the problem of cannabis

Biological evaluation of cannabis preparations

By Prof. G. Joachimoglu, Athens

The chemistry of cannabis is described in document E/CN.7/297.[1] Despite the great advances made in this field, we have so far no chemical method of determining the physiological effects of a cannabis preparation. That being so, pharmacological mehods must be used. I gather from such literature as I am acquainted with that S. Fränkel [2] was the first to carry out pharmacological experiments with cannabis on animals. He extracted 2.2 kg of resin from 10 kg of hashish with petroleum ether. The resin was subjected to fractional distillation at 0.5 mm/Hg. By repeated distillation at 215°C a light yellow liquid was obtained, which Fränkel called " cannabinol ". This should not be confused with crystalline cannabinol,[3] which is pharmacologically inactive, whereas Fränkel's cannabinol is active. Fränkel observed a characteristic intoxication pattern in dogs even after small doses. The cannabinol was given to the dogs orally either wrapped in meat or dissolved in oil. The animals became surprisingly quiet after one to two hours: " They immediately stop running around the cage and seem, to begin with, to lapse into a dreamy condition. A dog intoxicated with cannabinol is never heard to bark; only a few whimper after large doses. When moderate doses are given, the animals stand about the cage struggling, in a dreamy state, to fight off sleep. Now and then they will lift a front paw and try to grab an apparition in the air. In this condition the head is bent backwards and the eyes are directed towards imaginary objects hovering in the air. The intoxication develops slowly and, particularly after somewhat bigger doses, the animals freely adopt the most remarkably distorted postures. They will maintain for a long time any pose, no matter how uncomfortable, in which the experimenter puts them. At the hypnotic stage the animals stand about the cage fighting against sleep, their heads sinking lower and lower until their muzzles touch the ground. Then they start up, lift their heads again and let them drop once more as far as they can go, starting up again, and this goes on over and over again, often for an hour at a time, rather like a waking dream such as people experience on long railway journeys when they fall into a doze out of which they start at the slightest irregularity in the joltings — e.g., when the train passes over points — only to sink back immediately into their doze. Other animals stagger about the cage, generally falling head over heels. The animals react feebly to external stimuli and, as soon as they are left alone again, they relapse into their apparently very pleasant dream condition. After large doses they lie down and can hardly be got on their feet again." (S. Fränkel) So far as I know, it is only in dogs that cannabis provokes such a characteristic intoxication pattern.

K. D. Sargin & V. V. Vasilyeva [4] have made use of the absence of corneal reflex observed by Straub & Gayer in rabbits to assay cannabis preparations pharmacologically. After an injection of cannabis extracts the animals show a negative corneal reflex — i.e., when the cornea is touched, the eyelids do not close.

Difficulties arise in preparing an injectable extract. Sargin & Vasilyeva used cannabis resin dissolved in alcohol for injecting rabbits, while other authors prefer acetone solutions. The cannabis preparation (*Extractum Cannabis Indicae spissum*) is dissolved in slightly heated alcohol to produce a 1% solution. The volume injected intravenously is always 0.25 cc per kg of the animal's weight. Only the concentration of the preparation varies. A corneal unit is the smallest quantity of the preparation per kg of body weight that intermits the corneal reflex. It should be noted that the dose of alcohol injected does not of itself reduce the sensitivity of the cornea, and also that this method gives only approximate results.

The results of Sargin & Vasilyeva's experiments with rats and mice are interesting. With these animals, the intravenous injection of a 1% solution of cannabis resin in doses of 0.2 cc (or up to 0.5 cc for rats) produces no visible symptoms. Sensitivity to pain is not reduced. After injection of the aforementioned doses many of the animals, particularly rats, die.

G. N. Pershin [5] and E. A. Kechatov [6] have prepared emulsions from cannabis extracts and gave rabbits intravenous injections of them. Pershin's method is as follows : The weighed quantity of extract is dissolved in 10 parts of alcohol, 5 parts of powdered gum arabic being added to the solution. The sticky mass is then carefully mixed with water in a mortar until it becomes " runny ". More water is added to make up the desired volume. The dark-field microscope shows the emulsion to consist of small round particles, mostly less than 1 micron in diameter, with few larger-size particles 1-6 microns in diameter. It should be noted that the emulsion is very liqueous and passes through a Seitz filter without leaving any perceptible deposit.

Ketchatov used apricot gum in preparing the emulsion. A concentrated extract was obtained by macerating with alcohol (90%). This was dissolved in alcohol (1 : 1) and prepared with apricot-gum emulsions at varying concen-

[1] United Nations document E/CN.7/297, entitled " The possibility of replacing hemp fibre and hemp seed by other crops of similar industrial value or of developing narcotic-free strains of the Cannabis plant ", 24 March 1955.

[2] S. Fränkel, *Arch. f. experimentelle Pathologie u. Pharmakologie*, 1903, *49*, 283, quoted after Joachimoglu in A. Heffter's " *Handbuch der experimentellen Pharmakologie* ", vol. II, part 2, pp. 1114-1119.

[3] Document E/CN.7/297, p. 13.

[4] K. D. Sargin & V. V. Vasilyeva: " The Biological Assay of Cannabis Preparations ", *Pharmakologiya i Toxikologiya*, 1939, vol. 2, No. 4, pp. 63-66.

[5] G. N. Pershin : " The Pharmacology of Cannabis ", *Pharmakologiya i Toxikologiya*, 1949, vol. 12, No. 4, p. 37.

[6] E. A. Kechatov: " Cannabinol reactions and pharmacological analyses of the resinous secretions from Cannabis cultivated or grown wild in the northern Caucasus ", United Nations Document E/CN.7/352, 3 April 1958.

trations — viz., 2%, 5% and 10%. This author mentions that the cornea dose in Pershin's tests for extracts of *Cannabis Indica* was only 0.001 g per kg of body weight, whereas in his own tests it was: with a 2% emulsion (0.25 cc = 0.005 g resin) 5 times higher, with a 5% emulsion (0.25 cc = 0.012 g resin) 12 times higher, and with a 10% emulsion (0.25 cc = 0.025 g resin) 25 times higher. His conclusion is that " resinous substances contained in cultivated and wild growing plants showed that these substances do not have the same physiological effects as do the resinous substances derived from cannabis plants from India ". Why the cornea dose was so different depending on the strength of the apricot-gum emulsion applied is a difficult matter to explain. It should be noted that the resorption of the active constituents of an emulsion and its transmission into the central nervous system cannot be uniform. It is not customary in pharmacology to give intravenous injections of emulsions. *Corpora non agunt nisi soluta.* I am not aware of such differences being observed when using drugs dissolved in water or oil, as Kechatov found with cannabis.

It may be possible to dissolve the active constituents of cannabis in a neutral oil and to inject the solution intraperitoneally. With oily solutions of camphor, the full effects of the camphor can be observed very quickly.[7]

When making pharmacological tests to determine the effective dose for animals, it is absolutely necessary to use a standard preparation. This enables an accurate estimate to be made of the animal's sensitivity. Among those used are the digitalis preparations (leaves, tinctures, etc.). Without a standard preparation, no such estimates can be made.

With cannabis it is also important to test the corneal reflex quantitatively — i.e., to determine the strength of the stimulus applied to the cornea. For this purpose, von Frey's method can be applied. He used hairs of different thicknesses (0.05 – 0.1 mm). The weight required to produce the pressure that must be exerted to bend the hair is determined by means of a balance. If, for instance, this weight is 0.525 g and the hair is 0.07 mm thick, the pressure value of the hair tested is $\frac{0.525}{0.07} = 7.3$. Clearly, the higher the pressure value, the stronger the stimulus applied to the cornea. A series of hairs of increasing pressure value is used in order to find which produces a positive corneal reflex. In the case of a narcotic effect a hair with a fairly high pressure value will obviously produce such a reflex. Therefore, the sensitivity on the cornea will be tested with the hairs before the cannabis is given, and then compared with the sensitivity after various doses and intervals of time.

[7] G. Joachimoglu : *Archiv f. experimentelle Pathologie & Pharmakologie*, vol. *80*, 1, 1916.

Recapitulation

(1) The activity of cannabis preparations cannot so far be determined by chemical methods; pharmacological methods must be used.

(2) Cannabis produces a characteristic intoxication pattern in dogs. As any quantitative estimate of the active constituents of cannabis demands the use of many animals, a method in which dogs are used will encounter serious difficulties.

(3) The method using rabbits would appear to be more promising.

(4) In testing the corneal reflex in rabbits with the irritant hairs used in the von Frey method, the sensitivity of the cornea can be determined quantitatively.

(5) In any pharmacological method used for quantitatively determining the active constituents of a drug, comparison with a standard preparation is indispensable.

Experimental study relating to the antitussive properties of narcotine* hydrochloride

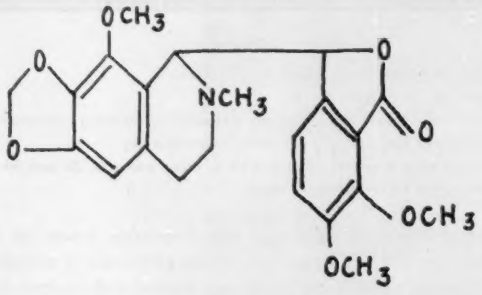
By Jean La Barre and Henri Plisnier
Pharmacodynamics Laboratory, University of Brussels

There is a high concentration of narcotine which may vary between 4% and 10%, in raw opium.

It is commonly used in medicine in hydrochloride form melting point 176°, almost insoluble in boiling water, alcohol and boiling chloroform, soluble in 22 parts benzene, 170 ether and 300 amyl alcohol.

Structurally it has a chemical relationship with hydrastine, differing from it only by the presence of a methoxy group in position 8. Physiologically it is among the isoquinoline derivatives, showing a constitution and antitussive properties similar to those of narceine, which was used as a cough cure as early as during the Second World War in the place of codeine, which was in short supply.

The probable chemical structure of narcotine corresponds to the formula given below.



It is therefore a benzoyltetrahydroisoquinoline.

The earliest pharmacological works attempted to define the analgesic properties of narcotine, in particular the studies made by Meissner (1913), which brought out the important point that massive doses of this alkaloid stimulate the bulbar respiratory centre and so to some extent act as an antagonist to morphine.

When examining the peripheral action of opium alkaloids, Macht, Johnson & Bollinger (1916) noted that, although narcotine has only a very slight analgesic effect, it displays an intensifying sedative property in association with opium. This intensification was also noted by Albright (1939) when studying the reflex stimulants producing pain in cats. This author also observed an intensification of the analgesic action of morphine when associated with narcotine. The local anaesthetic action on a rabbit's eye produced by cocaine is in no way intensified in animals treated with narcotine, according to Jürgensen-Stender (1936). Similarly Chopra, Mukerjee & Dikshit (1930) did not observe any lessening of peripheral pain after treatment with narcotine. Barlow & Stormont (1932), using narcotine as a pre-narcotic medication for rats, were unable to observe any intensification of the anaesthesia caused by inhalation of nitrogen protoxide. Many experiments have been made with the aim of proving that, both in therapeutic doses and in massive concentrations, this alkaloid has a stimulating effect on the respiration both in normal animals and animals which have been dulled beforehand by chloralose, barbiturate derivatives or morphine.

Chopra and his collaborators (1930) noted a stimulation of the exhalation and inhalation frequency after intravenous administration, and Van Dongen (1940), confirming the work of Meissner (1923), proved that narcotine to a great extent neutralizes post-morphine respiratory depression, without, however, causing animals in a state of narcosis to wake more quickly.

The blood pressure tends, according to Hayashi (1932), to fall slightly with small doses and to rise with massive concentrations, following the discharge of adrenaline, which, however, according to Mercier & Delphaut (1935), is of little significance compared with the reactions produced by laudanosine or papaverine. In connexion with this hyperadrenalemia, it should be mentioned that Ro (1935) also notes a moderate hyperglycemia phenomenon after the administration of a dose of 5 mg/kg to rabbits.

The studies carried out by Hanzlik (1921) and Sakussow (1929) on the heart, mainly *in vitro*, prove that narcotine has a depressive effect by direct action upon the myocardium, accompanied by an increase in the coronary flux.

One of us (La Barre, 1924) previously studied *in vitro* the action of narcotine on the motility of a rabbit's intestinal loop and showed that moderate doses of this alkaloid (1 to 5 mg) reduce the peristaltic movements, and that massive doses (10 mg) stop them completely. This would explain the constipating effect of massive concentrations of narcotine, since it, like morphine, very appreciably lessens the diffusion of choline from the whole of the intestinal mass by forming with it narcotine-choline complexes with a hypotonic effect on the isolated loop.

It should be pointed out, however, that, according to Zunz (1932), narcotine hydrochloride does not increase the period of gastric digestion in dogs, and differs notably in this respect from morphine and papaverine.

It should also be noted that, according to Usui (1937), uterine contractility appreciably increased under the influence of narcotine, as it did after the administration of morphine.

* Proposed international non-proprietary name : noscapine.

The works dealing with the antitussive effects of narcotine hydrochloride will now be considered more particularly.

Konzett & Rothlin (1954) found that doses of the alkaloid ranging from 0.1-1 mg/kg inhibit the cough reflexes in cats caused by mechanical stimulation of the tracheobronchial membrane. Moreover, it would appear to cause a bronchodilatation, whereas codeine and its derivatives tend to be bronchoconstrictors.

Other experimental work carried out on dogs and man by Winter & Flataker (1954), by Bickerman, Barach & Drimmer (1954) and by Green & Ward (1955) have shown that narcotine administered previously to an aerosol of sulphuric acid or of tartaric, citric and benzoic acid in varying concentrations has marked antitussive properties both in animals and in certain patients suffering from bronchial asthma. Useful applications of narcotine in human therapy were pointed out by Janschulte (1956) and by Bergmann & Stolzer (1956), whereas Gravenstein & Beecher (1954), using the ammonia and citric acid inhalation technique, obtained significant antitussive results only with codeine and heroin, narcotine being found no better than placebos.

A study of the toxicity of narcotine was undertaken as early as 1934 by Cooper & Hatcher, who reported that this drug does not remain long in the blood stream and becomes localized, more particularly at the level of the lungs, liver and kidneys. With cats there is some slight elimination through the kidneys.

After this general account of the works published on the pharmacodynamic properties of narcotine, the experiments we have been conducting with this drug for several years will now be described.

This study will concentrate mainly on:

(1) The respiratory and tensional effects of narcotine hydrochloride;

(2) The action of narcotine on the respiration of rabbits;

(3) The action of narcotine on induced cough;

(4) The action of narcotine on induced bronchial secretion;

(5) The tranquillizing effect of narcotine hydrochloride;

(6) The toxicity of narcotine.

Let us examine in turn the results observed during these various series of experiments.

A. *Action of Narcotine on the Respiration and Blood Pressure of Rabbits treated with Urethan*

We experimented on a batch of rabbits anaesthetized by intraperitoneal injection of a solution of urethan for changes in the carotid blood pressure (lower line of graph) and respiratory movements (upper line of graph) recorded by a tracheal cannula connected to a Marey sphygmograph.

We used doses of 2mg/kg, which are definitely higher than those used for curing coughs. By way of example, we are giving one of the graphs plotted under these conditions (fig. 1).

As can be seen from figure 1, a dose of 2 mg/kg narcotine induces a slight but prolonged hypertensive effect (lower line) and a marked deepening of the respiration (upper line).

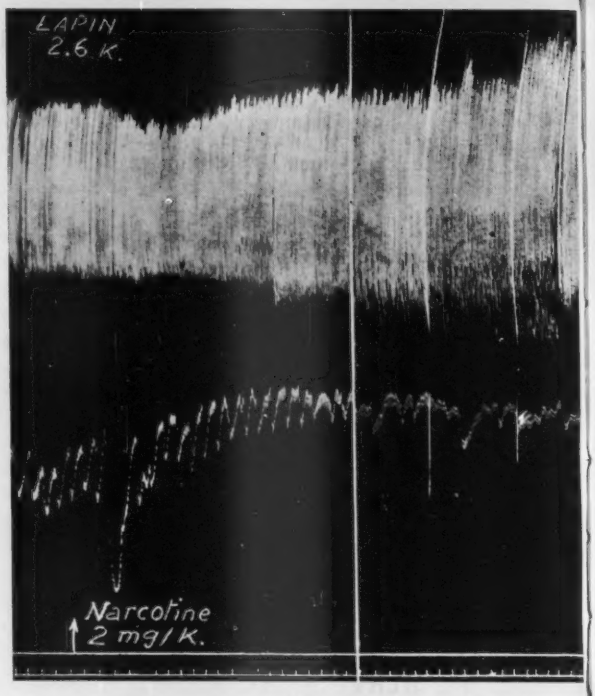


FIGURE 1

Rabbit weighing 2.6 kg treated with urethan.
Upper line: respiratory movements;
Lower line: Carotid blood pressure measured by mercury manometer;
Effect of injecting 2 mg/kg narcotine hydrochloride;
Time recorded every 15 seconds with a break every 10, 20 and 30 minutes after narcotinization began.

This hypertensive effect and this favourable action on the respiration differ completely from the properties of morphine and codeine, which depress the circulation and respiration.

B. *Action of Narcotine on Respiratory Capacity*

Plisnier (1957), in the course of a comparative study, investigated in particular the effects of opium derivatives on the posthistamine and postacetylcholine bronchospasm. The part of the study dealing with codeine is of special interest for our experiments.

He has, in fact, shown that an intravenous injection of 1 mg/kg codeine phosphate in dogs treated with chloralose invariably produces a considerably longer bronchospasm than the posthistamine or postacetylcholine control bronchospasm (fig. 2).

The fall in arterial tension after codeine treatment is equally important and it takes 20 minutes to return to normal with the dose used. Furthermore, the bronchial constriction continues after the phase of acute contraction, entailing a lessening of the respiratory capacity.

We have had an opportunity of showing that the bronchial constriction with other codeine derivatives, such as pholcodine, is particularly intense, as figure 3 proves.

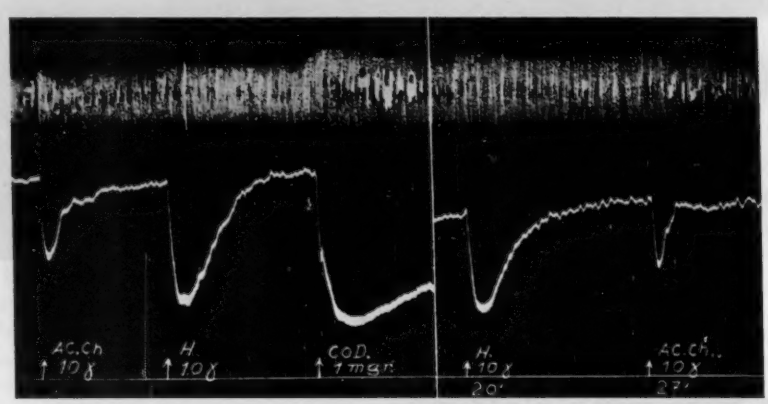


FIGURE 2

Dog weighing 10 kg treated with chloralose.
Bronchospasm induced by intravenous injection of 1 mg/kg codeine phosphate.

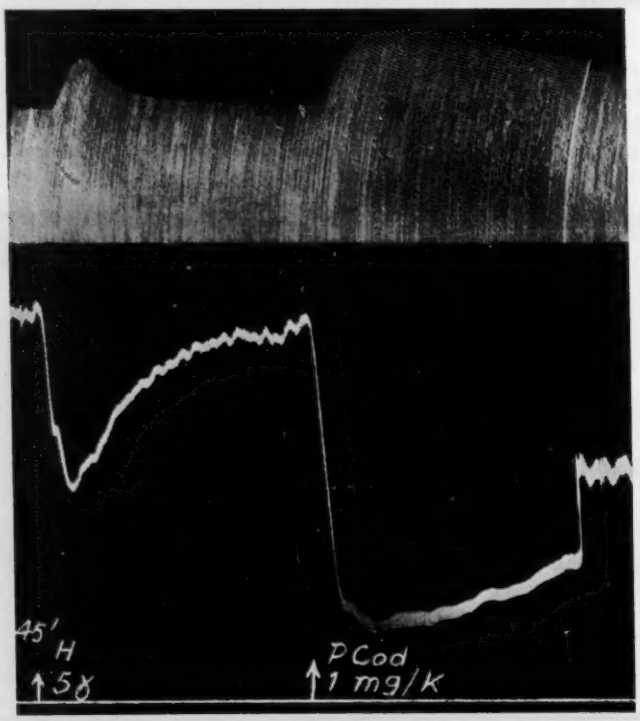


FIGURE 3

Dog treated with chloralose.
Upper line:
PCod: Bronchospasm induced by intravenous injection of 1 mg/kg pholcodine;
H. Histamine bronchospasm (dose: 5γ);
Lower line: Carotid blood pressure.

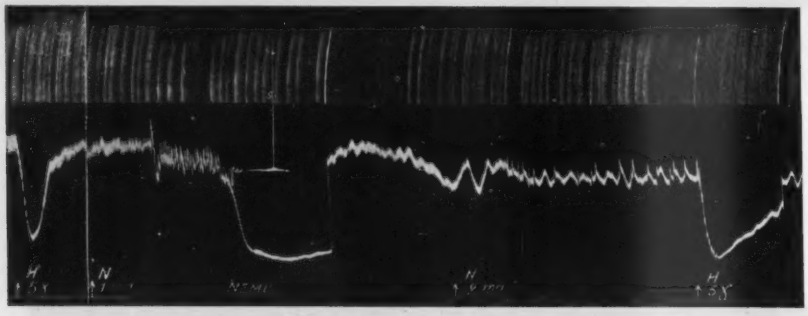


FIGURE 4

Dog weighing 10 kg treated with nembutal.
Upper line: Record of volume of air exaled;
Lower line: Carotid blood pressure;
H: Injection of a test dose of 5γ histamine;
N: Intravenous injection of 1 and of 2 mg narcotine.
Nemb: reinjection of appropriate dose of nembutal.

Let us now look at the results observed after administering a dose, also of 1 mg/kg, narcotine hydrochloride.

As in the previous experiments, we used the method described by Charlier & Vandersmissen (1954) — i.e., recording the carotid blood pressure and the changes in the air exhaled by dogs treated with nembutal.

We were thus able to compare the duration of the inhibiting effects of codeine (fig. 2) and narcotine (fig. 4).

As can be seen from figure 4, narcotine hydrochloride has the curious property of causing a marked and prolonged dilatation of the respiratory depth which, in practice, reflects over-capacity of the lungs.

We thus found that narcotine had a very favourable effect on bronchodilatation, contrasting strongly with the broncho constriction observed after administering codeine or certain of its derivatives.

C. *Action of Narcotine Hydrochloride on Induced Cough*

The methods described to obtain a specific cough reflex differ with the methods used to cause it. The cough reflex

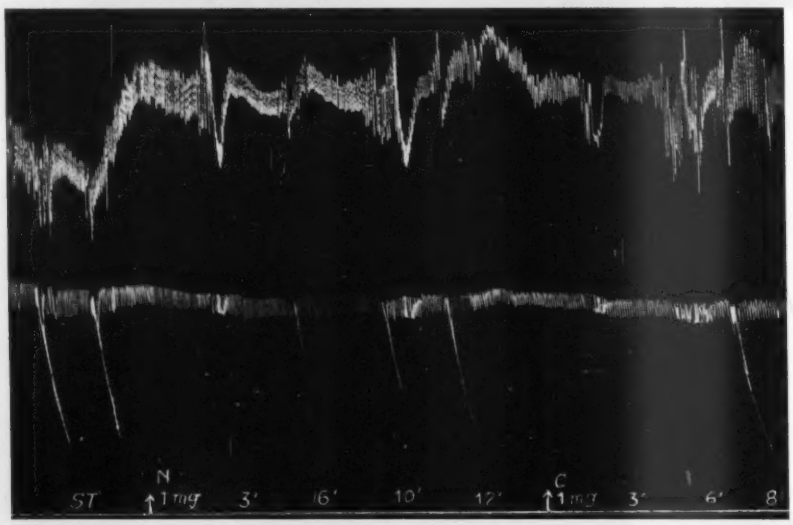


FIGURE 5

Cat weighing 2 kg 500 treated with nembutal.
Recording of the cough reflex (lower line) and of carotid blood pressure (upper line).
N: Effect of the injection of 1 mg narcotine hydrochloride;
C: Effect of the same dose of codeine.

was induced in turn by pleural irritation, by aerosol inhalation of irritant mists and by inflammatory irritation of the trachea following the use of chemical substances.

The drawback of these various methods is that it is not possible to assess the antitussive action of a given drug quantitatively, because the amount of the stimulant cannot be strictly dosed.

We preferred to use a technique based on Domenjoz' method (1952).

The method used was therefore to study in cats treated with nembutal the disappearance of the cough reflex induced by rhythmical stimulation of the upper laryngeal nerve under the influence of intrafemoral injection of either a dose of 1 mg/kg narcotine hydrochloride or the same concentration of codeine phosphate.

The electrical stimulation is renewed at the second, fifth, tenth and fifteenth minute and, subsequently, every two minutes, which makes it possible to measure the duration either of the stoppage or of the reduction of the cough reflex induced thereby.

We were thus able to determine the antitussive action of narcotine hydrochloride as compared with codeine. In these tests 1 mg/kg doses of narcotine and codeine were used.

As can be seen from figure 5, the duration of the stoppage or of the reduction of the cough reflex was 12 minutes for narcotine hydrochloride and 8 minutes for codeine phosphate.

By repeating the experiments it is possible to show that a dose of 0.75 mg narcotine hydrochloride is required to obtain a tranquillizing effect identical with that induced by 1 mg codeine phosphate.

D. *Action of Narcotine on Induced Bronchial Secretion*

We now come to the study carried out by Plisnier & Hernalsteen at the pharmacodynamics laboratory of the University of Brussels.

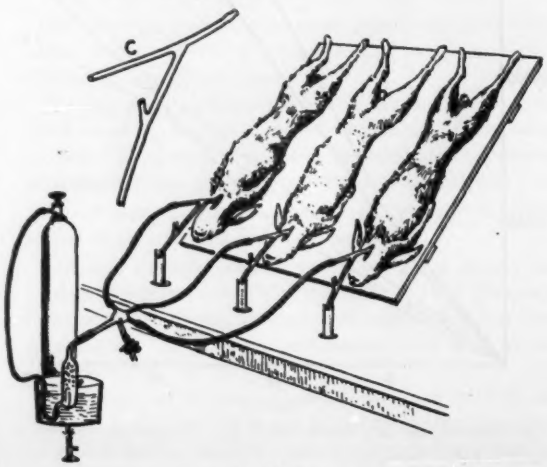


FIGURE 6

Plan of experiment for collection of bronchial secretions.
C: Cannula with four orifices.

Its purpose was to examine the action of narcotine hydrochloride on the bronchial secretion.

The experimental technique used was that of Perry & Boyd (1941), as improved by H. Plisnier (1956-57). The author used a method, the principle of which is reproduced in figure 6, the experiment being conducted on three rabbits to which 750 mg/kg urethan had been administered by intraperitoneal injection.

Since spontaneous inhalation of water vapour does not enable an adequate amount of secretion to be collected, H. Plisnier used a very fine aerosol which makes it possible to insert a special cannula (see fig. 6) into the respiratory orifice under the light and constant pressure of a mist kept at a temperature of 40°C. The pressure of air from a cylinder of compressed air operates a misting appliance, which is connected with the test animal's trachea by tubes of identical cross-section and length. Then, in order to promote the excretion of mucus, a polyoxyethyl polymer of paradiisobutyl phenolformaldehyde (superinone) in a solution of glycerine and bicarbonate is added to the physiological aerosol solution as a detergent.

In this experiment the centre rabbit, regarded as the control, is given only the physiological aerosol with superinone added and the rabbits on each side are given intravenous injection of 1 or 2 mg/kg narcotine hydrochloride after the first hour of treatment with an aerosol identical with that used on the control rabbit.

The amounts of mucus secreted by the three animals during the second hour are then observed.

Doses of 1-2 mg/kg narcotine induced in all cases a very marked increase in the volume of the bronchial juice collected.

The figures in the table below were obtained by calculating the average percentages of the variations in secretion observed during five series of similar tests.

TABLE 1

Test series	Dose of narcotine administered	Percentage of increase in the amounts of bronchial juice secreted by rabbits subjected		Percentage of difference compared with control rabbit
		to a physiological aerosol (control)	to the same aerosol used after administration of narcotine hydrochloride	
A	1 mg	20%	55%	+35%
B	2 mg	10%	51%	+41%
C	2 mg	75%	92%	+17%
D	2 mg	20%	85%	+65%
E	1 mg	20%	62%	+42%
Average				+40%

The diagram in figure 7 shows by way of example the results observed with three rabbits during a test in which the dose of narcotine administered was 1 and 2 mg/kg.

As can be seen from the above table and from figure 7, narcotine in most cases induces increases in bronchial secretion which may be estimated at approximately 40% of normal secretion.

It thus appears that compared with codeine, narcotine

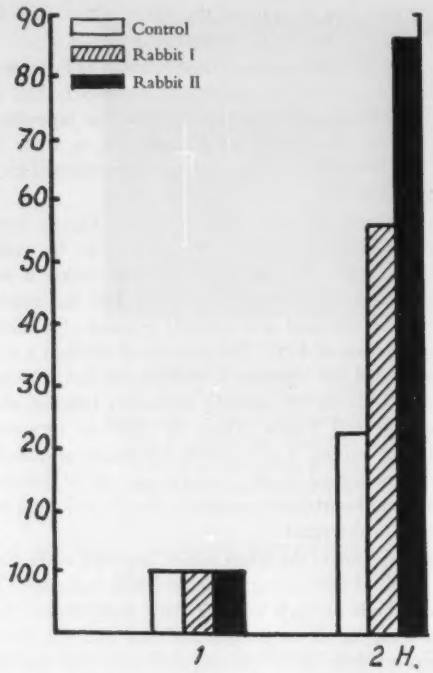


FIGURE 7

Action of narcotine hydrochloride on bronchial secretion.

The secretion collected during the first hour is rounded off to the value 100.

White column: Control rabbit;

Shaded column: Rabbit having received an intravenous injection of 1 mg/kg narcotine hydrochloride;

Black column: Rabbit having received an intravenous injection of 2 mg/kg narcotine hydrochloride.

hydrochloride has the great advantage of facilitating expectoration and stimulating the production of bronchial mucus.

E. *Tranquillizing Effects of Narcotine Hydrochloride*

As narcotine hydrochloride seemed to possess no specific analgesic properties, according to many authors, and as the salts of narcotine, like papaverine, cannot, according to Eddy (1957), be classed among the drugs liable to produce addiction, the WHO sub-committee concerned with devising international non-proprietary names has proposed that this substance should preferably be designated Noscapine. Nevertheless, we considered it desirable to find out whether this alkaloid possessed tranquillizing properties.

To that end we determined the tranquillizing effect of narcotine on rats, using the method described by J. J. Desmarez (1957), based on hourly changes in motility.

The experiment was performed with six pairs of white rats placed in six cages enabling the motility to be recorded by numeration.

The observation period was 2 days in the normal state, 2 days during the treatment with doses of 2 and 4 mg/kg of a 2% narcotine solution, and 1 day after therapy had been stopped.

The cumulative curves representing the motility of the rats noted by 6 hour periods in the normal state (1 and 2), during treatment (3 and 4) and during the day following the stoppage of treatment (5) are given in figures 8 and 9.

As can be seen from these curves, a definite tranquillizing effect, but a slight one compared with that observed with reserpine, sets in from the beginning of the treatment. With light doses of narcotine (2 mg/kg), if the normal motility is regarded as equivalent to 100%, it falls to 58% after 2 days' treatment.

With a strong dose of 4 mg/kg, motility is reduced only to 60% after 2 days' treatment.

According to these results, then, narcotine hydrochloride has definitely tranquillizing properties when administered in light doses, particularly for antitussive purposes, whereas by increasing the concentration a state of hyperexcitability appears to be induced, antagonistic to the tranquillizing effect which would otherwise set in.

Accordingly, it still seems worth while to stress the fact that narcotine hydrochloride in antitussive doses definitely possesses tranquillizing properties.

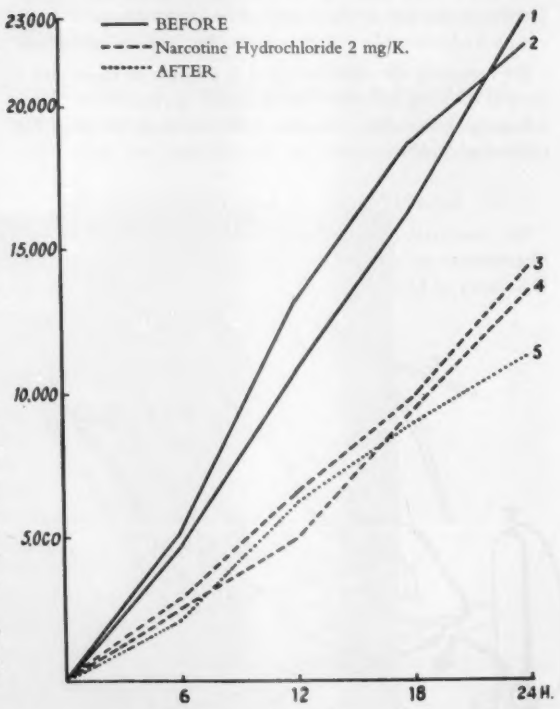


FIGURE 8

Curves showing the daily motility of six pairs of white rats.

1 and 2: Before treatment;

3 and 4: During 2 days of treatment with a dose of 2 mg/kg narcotine hydrochloride;

5: After treatment.

F. *Toxicity of Narcotine Hydrochloride and Codeine Phosphate*

The lethal doses for guinea-pigs were determined by Fubini for different derivatives of opium; the results were: thebaine 0.03 g, codeine 0.12 g, morphine 0.58 g, narcotine 0.60 g, papaverine 0.64 g per kilogramme of body weight.

According to these results, the toxicity of narcotine approaches that of morphine; but it has not been accurately determined for several kinds of animal, taking into account the speed of administering the drug to man. Chopra and his collaborators (1930) reported that with a dose 2-3 g, symptoms of nausea are observed, followed closely by vomiting and headache.

We pursued this study, using guinea pigs weighing 300-350 g all from one breeder and subjected to a constant diet. Several guinea pigs (8 to 10) were used to determine the lethal dose of the two drugs, codeine and narcotine.

The solution is injected at a speed and in a concentration such that death ensues in 12 to 15 minutes with an injected volume ranging between 12 and 15 cm^3 (Knaffl-Lenz' method, as modified by La Barre & Thomas (1947)).

To ascertain the lethal dose, the concentration of the drug leading to the stoppage of cardiac contraction is determined, this being made visible by using a cathodic oscillograph and a Hugues recorder. As a rule, the lethal concentration is reached when the animal ceases to breathe, and the heart shows three bands of silence on the oscillographic record.

By this process we determined the lethal dose of codeine phosphate, reckoned in codeine base, and the lethal dose of narcotine hydrochloride, also reckoned in base.

The average values found with 12 guinea pigs with 4‰ solutions were 106 mg/kg (lethal dose) for codeine base and 75.72 mg or 76 mg/kg (lethal dose) for a 25 mg‰ solution narcotine base.

General Considerations and Conclusions

During recent years, a great many experiments have been carried on to discover antitussive drugs belonging to two different groups of substances.

The first group included the opiates and their derivatives, which could be classified in the following order of decreasing potency : dihydrocodeinone, acetyldemethyldihydrothebaine, dextromethorphan and sodium diterbutylnaphthalene.

A second group (synthetic derivatives) comprises the derivatives of cyclopentane and carbetopentane.

Although the substances in the second group have a less marked antitussive action, they have the twofold advantage of reducing or stopping histamine and acetylcholine bronchospasms and of facilitating expectoration, while they do not cause addiction.

Narcotine and its salts, to which we have paid special attention in this study, although among the opium derivatives of an isopuinoline character, have the tremendous advantage of not giving rise to habituation and dependence phenomena, and have an antitussive efficacity of their own 50% higher than that of codeine.

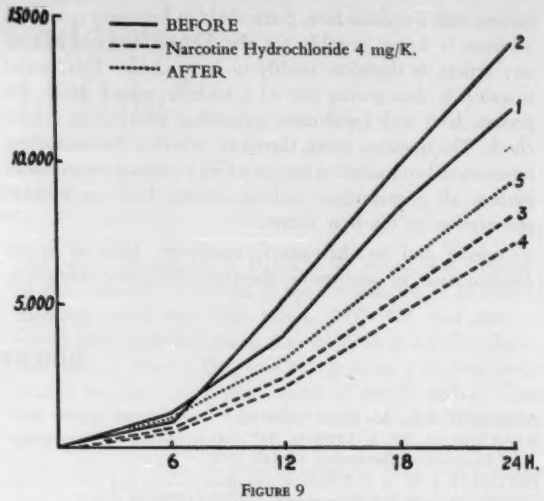


FIGURE 9

Curves showing the daily motility of six pairs of white rats.
1 and 2: Before treatment;
3 and 4: During 2 days of treatment with a dose of 4 mg/kg narcotine hydrochloride;
5: After treatment.

Furthermore, it should be pointed out that the salts and other derivatives of codeine in doses of 1 mg/kg regularly and without exception induce a long-lasting bronchospasm, frequently accompanied by a prolonged fall in tension.

In the supplementary study we have undertaken, we have also been able to show that narcotine in antitussive doses does not lower the blood pressure and that repeated doses may even stimulate respiration, offsetting the depress or effect of hypnotics such as chloralose or urethan and of barbiturate derivatives (pentothal).

Lastly, narcotine hydrochloride has the property of stimulating bronchial secretion in rabbits where the other opium derivatives, such as morphine and codeine, inhibit the excretion of mucus and thus totally fail to induce expectoration.

It is worth recalling that narcotine hydrochloride in antitussive doses has some slight tranquillizing properties, which are not actually hypnotic as are those of the barbiturate derivatives. The advantage of this benign and short-lived action is that it does not induce subsequent somnolence.

It should also be stressed that narcotine hydrochloride does not upset the gastric function and in concentrations used for antitussive effect does not produce constipation.

A very marked increase in the consumption of codeine has been observed during recent years, which cannot be explained by its more intensive use as a cough cure. This mania for codeine is increasing, as a result of the use of preparations combining codeine with other analgesics such as phenacetin, the effect of which is to strengthen the euphoria-producing properties of the codeine. As this kind of mixture can be obtained from druggists without a medical prescription, on account of the special regulations applicable to codeine preparations, the enormous increase in the use of these prepa-

rations with a codeine base, particularly in European countries, without it being possible for the control services to take any action, is therefore readily understandable. This special situation is thus giving rise to a codeine mania which the present laws and regulations governing pharmacies cannot check. The question arises, therefore, whether the competent international commissions may not find it necessary to consider putting all preparations with a codeine base on medical prescription in the near future.

Codeine and its derivatives, moreover, have so many disadvantages in antitussive thereapy (bronchoconstriction, slight hypotension, inhibition of bronchial secretion, unfavourable effect on the respiratory centre, constipating effect, etc.) that after the experimental study we have undertaken, we are tempted to propose the replacement of codeine by similar doses of narcotine, since narcotine does not produce addiction and has a more powerful action against cough. This proposal would be supported by the fact that the clinical work of Bickerman, Barach & Drimmer (1954) and the more recent work of Bergmann & Stolzer (1956) have already proved the efficacity of narcotine in the treatment of bronchial ailments in man.

BIBLIOGRAPHY

ALBRIGHT, I. C., *Acta Brevia Neerlandica de Physiologia, etc.*, *9*, 109, 1939.

BARLOW, O. W. & STORMONT, M. P., *Journal of Pharmacology and Experimental Therapeutics*, *46*, 141, 1932.

BELLVILLE, J. W. *et al*, Effects of noscapine, codeine and morphine on respiration, *Journal of Pharmacology*, *122*, 5A (1958).

BERGMANN, M. & STOLZER, H., *Wiener medizinische Wochenschrift*, No. 9, 1956.

BICKERMAN, H. A., BARACH, A. L. & DRIMMER, F., *American Journal of the Medical Sciences*, *228*, 156, 1954.

BICKERMAN, H. A. *et al*, The cough response of healthy human subjects stimulated by citric acid aerosol. Part II : Evaluation of antitussive agents. *American Journal of the medical sciences*, *234*, 191 (1957).

CHARLIER, R. & VANDERSMISSEN, L., *Archives internationales de Physiologie*, *62*, 433, 1954.

CHOPRA, R. N., MUKERJEE, B. & DIKSHIT, B. B., *Indian Journal of Medical Research*, *18*, 35, 1930.

COOPER, N. & HATCHER, R. A., *Journal of Pharmacology and Experimental Therapeutics*, *51*, 411, 1934.

DESMAREZ, J. J., *C. R. Société de Biologie*, *151*, 1988, 1957.

DOMENJOZ, R., *Archiv für experimentelle Pathologie und Pharmakologie*, *215*, 19, 1952.

EDDY, N. B., *Drug and Cosmetic Industry*, No. 31, 1957.

ENDERS, A. & SCHMIDT, L., Die reflektorische Tätigkeit des Husten- und Atemzentrums unter dem Einfluss von Papaverinhydrochlorid. *Archives internationales de Pharmacodynamie*, *114*, 446 (1958).

FUBINI, *Moleschotts Untersuchungen*, *12*, 563, 1881; *12*, 9, 1882; *13*, 116, 1883.

GRAVENSTEIN, J. S. & BEECHER, H. K., *Arzneimittelforschung*, *5*, 364, 1955.

GRAVENSTEIN, J. S., DEVLOD, R. A. & BEECHER, *Journal of Applied Physiology*, 7, 119, 1954.

GREEN, A. F. & WARD, N. B., *British Journal of Pharmacology*, 10, 418, 1955.

HAAS, H., Vergleichende Untersuchungen über Analgetika. *Archiv für experimentelle Pathologie und Pharmakologie*, *225*, 442 (1955).

HANZLIK, P. J., *Journal of Pharmacology and Experimental Therapeutics*, *14*, 445, 1921.

HAYASHI, M., *Japanese Journal of Medical Sciences. IV Pharmacology*, 6, 203, 1932.

JANSCHULTE, B., *Medizinische Klinik*, *50*, 1788, 1958.

JÜRGENSEN-STENDER, O., *Archiv für experimentelle Pathologie und Pharmakologie*, *181*, 237, 1936.

KASE, Y., Pharmacological studies on cough reflex. *Japanese Journal of Pharmacology*, *4*, 118 (1955).

KONZETT, H. & ROTHLIN, E., *Experientia*, *10*, 472, 1954.

LA BARRE, J., *Archives internationales de Pharmacodynamie et de Thérapie*, *29*, 179, 1924.

LA BARRE, J. & THOMAS, J., *Dosage biologique et contrôle des médicaments*. G. Thone edit., Liège 1947, p. 142.

MACHT, D. I., JOHNSON, S. L. & BOLLINGER, H. J., *Journal of Pharmacology and Experimental Therapeutics*, *8*, 451, 1916.

MEISSNER, R., *Biochemische Zeitschrift*. *54*, 395, 1913. *Zeitschrift für die gesam te experimentelle Medizin*, *31*, 159, 1923.

MERCIER, F. & DELPHAUT, J., *C. R. Société de Biologie*, *120*, 1234, 1935.

PERRY, W. E. & BOYD, E. M., *Journal of Pharmacology and Experimental Therapeutics*, *73*, 65, 1941.

PLISNIER, H., Etude comparative de l'action des dérivés de l'opium et de diverses substances synthétiques à effet non morphinique sur le mécanisme de la toux, sur le bronchospasme et sur la sécrétion bronchique. Thèse d'agrégation, Bruxelles, 1957 : *Travaux de l'Institut de thérapeutique*, *39*, 1956-57 (p. 27-29).

RO, A., *Japanese Journal of Medical Sciences IV : Pharmacology*, *9*, 59, 1935.

SAKUSSOW, W. W., *Archiv für experimentelle Pathologie und Pharmakologie*, *144*, 331, 1929.

USUI, T., *Japanese Journal of Medical Sciences IV: Pharmacology*, *10*, 116, 1937.

VAN DONGEN, K., *Archives internationales de Pharmacodynamie et de Thérapie*, *64*, 494, 1940.

WINTER, C. A. & FLATAKER, L., *Journal of Pharmacology and Experimental Therapeutics*, *112*, 99, 1954.

ZUNZ, E., *Eléments de Pharmacodynamie spéciale*, Masson édit., Paris 1932, I, 184.

Barbiturate intoxication and addiction as a public health problem in Oslo *

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An essential prerequisite for obtaining reliable information about the frequency of the various forms of drug addiction in a population group is that suitable case-finding methods which are both accurate and cheap should be available. Until a comprehensive investigation of a representative group has been made by such methods, any assumptions we may make as to the extent of the drug addiction problem in the community are bound to be based on conjectures and therefore unreliable.

The difficulties in getting such a mass investigation of drug addiction carried out in a representative population group are almost insuperable, if only because it cannot be expected that the kind of intimate psychiatric examination required, including corroborative information from the patients' relatives, will be possible in the case of persons selected at random. At the present time, this sort of investigation represents the best available case-finding method.

To provide something potentially useful in the absence of such a method, we thought it might be worth while investigating the extent and the social consequences of drug addiction over a two-year period among the patients of an internal medicine department of a hospital where in-patients suspected of suicidal tendencies or drug addiction must be assumed to be willing to agree to a thorough psychiatric examination by psychatrists attached to the department as members of the medical staff. With a psychiatric service closely linked to a medical department in this way, there is less likelihood of any drug addiction case admitted on other grounds failing to be recognized.

As it seemed likely *a priori* that many of the patients admitted to the ward for treatment of acute narcotic intoxication would prove to be drug addicts, we shall deal first with this category of patients principally from the psychiatric point of view.

Acute Cases of Barbiturate Intoxication

A long series of investigations have shown that barbiturates are the means most frequently employed in cases of suicide, or attempted suicide. In England and Wales, for example, eight times as many persons committed suicide by means of barbiturates in 1954 as in 1945 (1). In most statistics of attempted suicide at the present time barbiturate intoxication accounts for about 70% of the cases. It is therefore natural that attempted suicide cases should primarily be placed in the internal medicine ward. Lingjærde & Römcke (2) found, for example, in their research on changes in the composition of an internal medicine ward over the period 1935-1952 that narcotic intoxication cases had more than doubled in number during that time — from 0.75% to 1.6%. It seems clear that barbiturates are the commonest means of suicide today. There are many reasons for this. The range of their therapeutic effectiveness is relatively narrow. The dose needed to induce tranquillity or sleep in persons suffering from acute anxiety is not much below the dose which, unless treatment is given, produces fatal intoxication. Barbiturates represent a painless method of suicide. In addition they are within reach of most potential suicides because they are widely used in psychic illnesses. It is difficult to say whether the absolute figures for suicide and attempted suicide have increased because barbiturates are easily accessible in so many homes, but Wiingaard (3) may be right in asserting that whereas at one time domestic rage was vented on the crockery, people nowadays take a pull at the medicine bottle.

Relatively few studies have been made in Scandinavia which throw light on the psychiatric aspects of cases of attempted suicide with barbiturates admitted to internal medicine wards. Dahlgren's findings (4) cover not only internal medicine departments of hospitals, but also psychiatric departments, which accounts for the high incidence of psychoses (35%).

Nor do Krane's (5) researches cover data on intoxication which can be regarded as typical of an internal medicine ward. Krane reviews the cases of attempted suicide admitted to Ullevål hospital between 1940 and 1948, and referred for polyclinic psychiatric examination. Only a fraction of attempted suicides are subjected to such examination.

Ettlinger and Flordh (6) carried out a psychiatric examination of 500 attempts at suicide among 457 patients who were at one time or another admitted to various wards of Söder hospital. They found that barbiturates were used in 73% of instances. In 58% of the cases of attempted suicide, the patient's condition was dangerous, in 34% it was felt that the patient needed to be kept under observation, and only 7% of the cases were regarded as harmless. The majority of cases were in the 20-40 age group, and were either divorced people or persons receiving public assistance. The most frequent causes of suicide were found to be conflicting passions, generally sexual or domestic in character. Other common causes were abuse of alcohol, economic troubles and housing difficulties.

In 66% of the cases, personality disorder symptoms were present. The men generally showed lack of moral fibre and

* On the subject of barbiturates, see *Bulletin on Narcotics*, vol. IV, No. 3: WHO Expert Committee on drugs liable to produce addiction; vol. VIII, No. 2: Report of the Interdepartmental Committee; vol. VIII, No. 3: Illicit traffic in narcotics; vol. IX, No. 1: WHO Expert Committee; vol. IX, No. 2: Abuse of barbiturates. The problem of barbiturates in the United States.

a psychopathic condition; the women immaturity and emotional instability. Fifty per cent of the cases were transferred to the psychiatric ward.

The rest of the material available from non-psychiatric departments does not cover cases which have undergone systematic psychiatric examination; in some instances, the compilers themselves call attention to this lacuna, especially where the purpose is to analyse the motives underlying attempted suicide and the seriousness of the attempt. Matrimonial and sexual conflicts seem universally to be a frequent cause of attempted suicide, especially among women.

Method used

We have gone through the case histories of patients admitted to ward IX, Ullevål Hospital, between 1 November 1955 and 31 October 1957, where the diagnosis was narcotic intoxication.

Since 1 November 1955 a regular system of psychiatric care has been operating in ward IX. One or other of the house physicians or assistant physicians in the psychiatric department for men has been assigned to ward IX for a period of six months at a time on a half-day basis. The psychiatrist is taken on to the strength of the medical ward, takes part in the examination of new patients, and is considered by both patients and staff as one of the ward doctors. By going through the case records and interviewing the incoming patients, the psychiatrist forms his impression as to which patients need psychiatric attention. The doctor in charge, the house physician or the assistant physician may order special psychiatric examination for patients who during their stay in the ward appear to need it. This system means that more patients are given psychiatric study than under the previous system when there was only a polyclinic service. Out of a total of 3,751 patients treated during this period of two years, 606 in all, or about 16%, were subjected to such examination, whereas under the old system with the polyclinic service, only about 4% were similarly examined.

As a regular practice, all cases of poisoning are sent for psychiatric examination. The only exceptions are cases of obvious accident or clearly unintentional intoxications where the patient is discharged at once. The fact must also be considered that some of the patients are admitted while the psychiatrist is away on holiday. The type of psychiatric examination carried out has been, on the whole, more thorough than is usual with the general polyclinic examination. The actual conversations with the patients have been longer and the psychiatric case histories which are written up have on the whole been on a par with the basic case histories in the psychiatric observation ward. In addition, conversations between the patient and the psychiatrist are often incorporated in the case history; and wherever possible, corroborative information has been obtained, and some of it is of decisive importance in getting anywhere near to the real situation in the case of patients in whom the conscious or unconscious play of fantasy is more evident than with most other psychiatric or internal medicine cases. In a number of instances supplementary information is obtained from the psychiatric departments in Ullevål Hospital.

The barbiturate content of the serum is determined by a spectrophotometric method described by Per Lous (7). The results obtained by this method for N-methyl derivatives such as Enheksymal are insignificant or negative.

Findings

Acute Cases of Barbiturate Intoxication

Frequency

During the two-year period covered by the study, 207 cases admitted to the ward, or 5.5% of the total admissions, were diagnosed as narcotic intoxication. Of these 207 cases, 137, or about 66%, were cases of barbiturate intoxication.

Distribution by Age, Sex and Marital Status

The cases of acute barbiturate intoxication comprised 81 women and 56 men; 63 were married, 37 unmarried, 24 divorced or separated, and 13 widowed. The age distribution is shown in table 1. There does not seem to be any indication of predominance of a particular category, except that of the patients under twenty, all six were women.

Table 1

Age and sex distribution of 137 barbiturate intoxication patients

Age group →	Under 20	20-40	40-60	60-70	Over 70	Total
Female	6	25	40	7	3	81
Male	0	16	33	4	3	56

Drugs used

In 35 cases (26%) it was impossible to obtain accurate information about the type of barbiturate used. The diagnosis of barbiturate intoxication in these cases was based on the presence of barbiturates in the serum. In 34 cases, the drug used was Pentymal (5-ethyl-5-(3 methylbutyl)-barbituric acid), in 30 cases Allypropymal (5-allyl-5-isopropylbarbituric acid) and in 6 cases, Hexobarbital (5-methyl N-methyl-5-cyclohexanyl-barbituric acid). Slower-acting barbiturates were less often employed. Fenemal (5-phenyl-5 ethylbarbituric acid) was used in 13 cases and Diemal (5-diethyl barbituric acid) in one case. Analgesics with a barbiturate content, generally Diemal or Fenemal, had been taken in 17 cases. In 9 cases, barbiturate intoxication was combined with another narcotic, usually of the morphine type. In 37 cases, alcoholic intoxication was diagnosed at the same time.

Barbiturate Concentration in the Serum

In 35 cases, no barbiturate content in the serum was established. These were mostly slight cases where during anamnesis reliable information that barbiturates had been taken was available. In 14 cases, the test was negative. The patients had taken fast-action drugs, and had been sent to hospital relatively late. In 7 cases, only traces of barbiturates were found. The other 81 patients showed positive quantities averaging 3.4 mg/100 ml, all except 4 being less than 10 mg/100 ml. The highest figure was 30.5 mg/100 ml in a patient who died shortly after admission. In 26 patients, who were comatose

when admitted, the barbiturate concentration, where known, averaged 3.6 mg/100 ml.

Somatic Therapy

The medical treatment proper was of the kind which is now common. Where not too long a time has elapsed since the barbiturate were taken, aspiration is carried out, with a ventricular lavage and use of carbon granulate where necessary. The anaesthetist is often called in to ensure that the air passages are free, and to assist his colleagues generally. Anti-shock therapy with control of the fluid balance and supply of oxygen is of vital importance. Treatment of the patient with antibiotics and change of surroundings are part of the general therapy. Analeptics of the old type were not used. But in 10 cases, beta-ethyl-beta-methyl-glutarimid and 2,4-diamino-5-phenylthiazol hydrochloride were used.

In 37 cases, the patients were comatose when admitted, and 20 of them showed clear signs of shock. Aspiration was carried out in 47 cases. The anaesthetist was called in to 20 patients. In 14 cases, the treatment was considered decisive in curing the illness and possibly in saving the patient's life.

Mortality

Seven patients — 2 women and 5 men — suffering from barbiturate intoxication died (ca. 5%). Their average age was 66.6 years, the youngest being 57 and the oldest 86. Two of the patients had taken Allypropymal, and 3 had taken barbiturates " with lasting effect ". In 2 cases, the barbiturates used were unknown, and 2 of the patients who died were suffering from incurable diseases of which they were aware (myelomatosis, cancer of the prostate with metastasis).

Psychiatric Diagnoses

In all, 117 of the 137 cases of barbiturate intoxication were examined by psychiatrists. The method of diagnosis used is multi-dimensional like that employed at the psychiatric clinic for men, Ullevål hospital. This means not only that the diagnosis is made on the basis of the most salient characteristic in the actual clinical condition (reaction diagnosis), but that an effort is also made to determine the underlying personality (personality diagnosis) and the circumstances which may have been decisive (situation diagnosis). The psychiatric diagnoses are set forth in table 2.

TABLE 2

Psychiatric diagnoses of 117 patients admitted to hospital with acute barbiturate intoxication

	Females	Males
Personality diagnoses		
Psycho-infantile and hysteriform persons	26	9
Persons with no apparent abnormalities	19	7
Psychopaths (self-assertive, unbalanced, hysterical, feeble-minded)	7	8
Persons lacking in self-control	4	12
Persons suffering from an organic brain disease	4	4
Intellectually handicapped persons	5	1
Other personality types (schizoid, cyclothiamic, asthenic, hyper-sensitive, dysphoric)	6	6
Reaction diagnoses		
Depressive neuroses	24	2
Hysterical reaction	25	3
Chronic alcoholism[a]	4	8
Abuse of alcohol and drugs[a]	7	20
Abuse of drugs[a]	7	10
Constitutional psychoses	1	1
Other diagnoses (alcoholic psychosis 1, arterio-sclerotic psychosis 1, epilepsy 1, melancholia 1, amentia 1)	3	2
	71	46
Situation diagnoses		
Erotic conflict	36	10
No decisive circumstance	9	18
Feeling of loneliness	6	2
Family difficulties	8	2
Complications of life	7	4
Difficulties at work	0	2
Financial difficulties	1	1
Physical malady or handicap	2	3
Social degradation	0	3
Death of close relative	2	1
TOTAL	71	46

[a] Of the alcohol and drug addicts, 10 also had a diagnosis of depressive neurosis, 1 a hysteric reaction, 1 a diagnosis of delirium and 2 of behaviour disorders.

Interpretation of the Significance of the Suicide Attempt

It may be difficult to decide whether the attempt at suicide was made in earnest, whether the poisoning is an attempt by the patient to convince his relatives of his suicidal intentions, or whether a pure " accident " has occurred. We therefore confined ourselves to a close investigation of those patients who had undergone a psychiatric examination. We found it relatively simple to exclude cases where on the whole it was not the patient's intention to poison himself, although of course from the viewpoint of depth psychology an apparent " accident " may perhaps still conceal unconscious death wishes. Proceeding on this principle, we concluded that in 27 of the 117 cases examined there was probably no real intention on the patient's part to commit suicide or to make his relatives believe that his life was in danger. Thirteen of these 27 were cases of overdoses taken by addicts. (By acquiring a tolerance to the drug, the addict has to take larger and larger doses in order to reach a state of euphoria, and he may find himself taking so much that he loses consciousness.) In a state of alcoholic intoxication, too, a patient may continue taking tablets till he becomes unconscious. This was what happened in 10 of the 27 cases. In 4 cases the accident happened in a state of sobriety. One case was an instance of the phenomenon which has been called " tablet automatism " or " serial consumption " (8), a process which is certainly more frequent than diagnosis can show. Now and then when barbiturates fail to induce sleep a sort of twilight zone can envelope the patient so that he does not remember that he has already taken the medicine in the prescribed dose. It may thus happen that without realizing the fact he takes all the tablets within reach. A wrong diagnosis of suicide may then be made if he does not wake up, since in actual fact what has happened is an accident. If he regains consciousness, he will as a rule be suffer-

ing from amnesia as regards the period when he was half conscious, and will not even be aware if the act of swallowing the tablets was due to suicidal intentions at a certain stage. Ettlinger & Flordh (6) came to the conclusion that this was the situation with ca. 28% of 365 attempted suicides using barbiturates.

In the 90 cases where it may be assumed that there was either a genuine suicidal intention or else a wish on the part of the patient to make others believe that he had suicidal intentions without endangering his own life, we tried to evaluate the seriousness of the problem underlying the patient's attempt at self-induced intoxication. This is extraordinarily difficult to assess, and the psychiatrist's opinion will often be decisive. We assigned these patients either to the group consisting of mainly serious attempts at suicide or to that consisting of attempts mainly not seriously intended. Actually, it often happens that the one intention does not exclude the possibility of the other existing at the same time, so that the attempt will be doubly motivated. A "successful" suicide is often the expression of a death wish in the patient, but this does not rule out the possibility that the motive was also to evoke a definite sympathetic reaction in one or more of his relatives. This latter motive will make itself felt, however, to a more considerable extent in patients who do not have really serious intentions. The factors we took into account in making this difficult distinction are as follows (in itself each is inconclusive, but taken together they are significant): the patient's pre-morbid personality; the question whether he has taken steps to ensure fatal results (closed doors, tablets taken in an isolated spot, etc.); the size of the dose; and the patient's emotional reaction to the intoxication when he recovers consciousness. The size of the dose, however, is not an absolute guarantee that the suicide attempt was serious, since it cannot be presumed that the patient has a sufficient knowledge of pharmacology to know what constitutes a fatal dose. It sometimes happens that the results are fatal even though the patient had no real suicidal intentions. On the other hand, there may be quite serious intentions underlying an attempted suicide which is not medically dangerous.

The attempts which were on the whole not serious in the case material available to us cover 64 patients (42 women and 22 men). The personality diagnosis in 29 cases (22 women and 7 men) was psycho-infantilism. The reaction diagnosis in 30 cases (24 women and 6 men) was hysteria. The most frequent situation diagnosis — in 29 women and 8 men — was sexual conflict, using the term in the widest sense, so that matrimonial conflicts fall under this head. Of these patients, 5 women and 5 men had already previously attempted suicide.

The patients who had seriously attempted suicide numbered 26 (17 women and 9 men).

In this group there were several whose personality had been regarded as in no way peculiar hitherto (11). The most frequent reaction diagnosis (in 16 cases) was depressive neurosis. Four patients were psychotics (constitutional psychosis in three cases, melancholic depression in one). In 6 cases, the diagnosis was chronic alcoholism and drug addiction, with a hysteric reaction. Sexual conflict was the determining factor in 9 of these patients, while in 9 others the cause was loneliness, the death of a near relative or the complications of life. There were evidence of previous attempts at suicide in 7 cases.

From the medical angle, 4 of the 64 not seriously intended suicide attempts were assessed as critical, 38 as requiring observation, and 22 as not dangerous. The corresponding figures for the 26 serious attempts were 8, 16 and 2.

Measures to be taken

In many cases the attempts at suicide were comparatively innocent, and it could very quickly be established that there was no continuing danger of suicide. Thus, the duration of hospitalization amounted to only 3.9 days per patient, and in most cases vigilance could be relaxed after the psychiatric examination.

In some cases, the patients were so violent that the police had to be called in. For a medical department, this was a most unfortunate occurrence. The reason was partly that the patients were continually in need of medical observation and therapy, and partly that there were difficulties in regard to space in the psychiatric wards.

Of the patients subjected to psychiatric examination, 19 were transferred to the psychiatric department. Some of them declined to move, a frequent reason given being that it was a form of discrimination to house them in a psychiatric ward, or that they had not the time for a long stay in hospital.

Because of the limited time at the psychiatrist's disposal in the medical department, which obliges him to confine himself essentially to the task of diagnosis, there was little time for psychotherapeutic conversations. However, these were held as far as was possible. Often the psychiatrist's initial conversation with the patient was of therapeutic value. In many cases, therapeutic treatment is given in consultation with the family, often the very people whom the patient would have hurt if the suicide attempt had succeeded. The critical situation, in conjunction with the attempted suicide, is often a favourable starting point for significant action which may prevent further reaction of the same kind. In many cases, we advise the patient to consult a private psychiatrist. Where the social situation was a considerable factor in the patient's breakdown, the social worker attached to the department was the one to institute rational therapy measures.

"Intoxication" following Therapeutic Doses

Among our case material we found three patients whose condition could be regarded as having been aggravated by therapeutic doses of barbiturates, so that hospitalization was necessary. All three cases were elderly women over seventy. Two were admitted for apoplexy. Both had been taking therapeutic doses of Allypropymal every evening for some months. They were somewhat confused mentally on admission, but recovered their faculties after two or three days. In one of them, the serum showed a barbiturate concentration of 9.9 mg/100 ml; in the other, there were only traces. The third woman had become mentally confused and incapable of work after taking therapeutic doses of Fenemal for three weeks. The barbiturate content in the serum was 4 mg/100 ml

when she was admitted; she recovered her faculties after the barbiturates had been discontinued.

It would seem that barbiturates are particularly unsuited as sleeping tablets for the elderly, as Aamodt (9) and Gaustad (10) have pointed out.

Is Barbiturate Intoxication a Frequent and Important "Internal Medicine Ailment"?

The reason why in our case material acute intoxication accounts for as much as 5.5 % of all cases admitted to hospital, as compared with 1.5% in Lingjærde & Römcke's (9) material is perhaps essentially the frequency of intoxication in combination with drug addiction and alcoholism in a large city as compared with small towns and rural districts. Particularly among the relatively few youngish patients admitted to internal medicine departments today, there are many cases of intoxication. In fact, our forty-one patients under forty years of age with acute barbiturate intoxication constituted 18% of all the patients under forty admitted to the ward during the two-year period. *Thus, one out of every five patients under forty is admitted to an internal medicine department as a result of a dangerous somatic condition in which psychic origin is clearly evident.*

In contrast with the data on successful suicides, in the material we compiled women are more numerous than men — in fact, there are about twice as many of them — both among the predominantly serious attempts at suicide, and among the predominantly not seriously intended attempts. Amongst our unsuccessful suicides there were also relatively far more younger people than in the statistics on actual suicide.

The mortality from acute barbiturate poisoning has fallen in the last twenty years from 20% to 3-6%. There is little likelihood that it can be further reduced, since there will always be some cases where the patient has taken such large doses, or where so long a time has elapsed before hospitalization that their lives can no longer be saved. The mortality figure of ca. 5% in our material is not so much higher than that reported from Bispebjerg Hospital (17, 18), and can be attributed to chance factors such as the patient's age, the type of preparation mainly used, and the length of time that elapsed before treatment was begun. The fact that in acute barbituric poisoning the prognosis is so much better today than twenty years ago is not exclusively the result of more effective therapy. It is probable that nowadays relatively slight cases of intoxication admitted to hospitals are more numerous, partly because the predominantly not seriously intended suicide attempts appear to have increased in frequency, and partly because today barbiturates with an effect of short duration are used more than before and the prognosis for these is better than in the case of barbiturates which are slowly eliminated. The high average (66.6 years) of the fatal cases is to be ascribed partly to the fact that serious attempts at suicide are more frequent among the elderly and partly to the fact that, in general, older people tolerate intoxication less easily. Apart from that, our experience tallies with what is generally recognized — namely, that mortality is greatest in men, in persons who have used barbiturates with a lasting effect and in those who have strong reasons for committing suicide (2, 4, 6, 7).

The relative frequency of barbiturate intoxication as a result of overdoses of analgesics with a barbiturate content (17 cases, one of them fatal) may be taken as an indication of the widespread use of such preparations. Barbituric analgesics sold in Norway all contain barbiturates with lasting effect, mostly Diemal and Fenemal; this makes them unusually dangerous as means of suicide. The pharmacological theory behind such a combination as a means of increasing the pain-relieving effect of, for example, phenacetine, is extremely doubtful. Boreus & Sandberg (11, 12), in an investigation carried out with experiments on animals, found that Diemal in relatively large doses has a negative effect on the antalgic properties of phenacetine. There is every justification for requiring producers of these combined antalgics to get rid of the barbiturate component or, at any rate, to replace it by a barbiturate which is quickly eliminated.

Our results show an astonishingly high percentage of barbiturate intoxication cases in barbiturate addicts who were responsible for 44 out of 117 cases.

If we include the 12 cases diagnosed as chronic alcoholism, there were in all 56 addicts in our case material. Thus, as half the patients admitted for acute barbiturate intoxication are either addicts or chronic alcoholics or both, the relatives must be called in as a routine procedure to provide corroborative information, since any further step would otherwise be unrealistic.

The prevalence of drug addiction and alcoholism and the frequent combination of barbiturate intoxication and acute alcoholic poisoning are explicable on several counts. Some were heavy drinkers before they started taking barbiturates; others had taken barbiturates to excess as a result of deprival symptoms, thus bringing on acute poisoning. On regaining consciousness many had no idea what had induced them to take so many tablets. Under the narcotic effect of barbiturates and alcohol suicidal impulses and also other undesirable impulses of which the patient when sober is himself unaware come to the surface. The impaired judgement and the increased tendency to unconsidered affective reactions consequent upon intoxication also perhaps play their part. In cases where barbiturate addicts have taken overdoses, the intoxication is strictly unintentional. The tolerance of the cerebrum for the drug results in the addict being obliged to take bigger and bigger doses to achieve euphoria. In the end, the hopeless economic and social situation in which he finds himself may prove decisive in bringing about an attempt at suicide.

Among the *predominantly serious attempts*, there was the same preponderance of women as among the predominantly not serious attempts. About a quarter of the cases of predominantly serious attempts had already tried, in most cases seriously, to commit suicide. Moreover, in a relatively high proportion of cases, the personality had not previously been peculiar. The suicide attempts in this group may be regarded as one of many manifestations of serious mental illness; thus, psychosis was diagnosed in 4 cases, and depressive neurosis

— more often than not with trauma of a more or less decisive kind — in 16 cases. Only 2 of these 26 serious attempt cases were regarded as medically not dangerous. The " seriousness " of these intoxication cases may be questioned on the grounds that the patients had after all arranged things in such a way that they were found and given treatment. This only means that the will to live was stronger than the urge to self-extinction. The motivation of such a serious step is understandably enough often ambivalent. But it is true of the group as a whole that as far as the patient himself was concerned, the will to commit suicide was experienced as something real, and that self-extinction may more often be regarded as an aim in itself and not as a means to influencing the attitude of relatives. Surprisingly often it was the feeling of loneliness, of being unwanted and useless, the lack of a sense of belonging to a group or, as it has been called, " excommunication ", that was the fundamental cause of desillusionment. In accordance with the greater seriousness of the underlying psychiatric trouble, a relatively large number of these patients were transferred to the psychiatric wards, where for the most part they were kept on for psychotherapeutic conversations, and strongly advised to visit a psychiatrist after discharge.

Even though it transpired from the psychiatric examination of these patients that the attempt at suicide must be regarded as seriously intended, many of them were not considered as still having suicidal tendencies. There were many reasons for this apparently illogical conclusion. It is not uncommon for the very fact of having stood at the threshold of death in this way to have a salutary effect on the patient's psychosis. Moreover, the serious attempts at any rate will finally convince the relatives that the patient is really ill, so that their attitude changes in a direction favourable to him.

It is remarkable that in the whole of our case material there was not a single case of anxiety neurosis, and that there was only one case of depression which might have been connected with a manic-depressive condition. As pointed out by Levine (13) and others, melancholia as such accounts for only a very small fraction of potential suicide cases. Thus, while it is always correct to associate the concept of melancholia with the danger of suicide, the converse is not equally true, because suicide and, more particularly, unsuccessful suicide attempts are so frequent among patients who are not melancholics.

As was to be expected, in a body of material on cases where psychiatric investigation of the intoxication was regularly carried out, a considerable number of them were assessed as " predominantly not seriously intended ". About two-thirds of our patients were considered to be in this category. Their average age was lower; they included a greater number of cases which, from the medical point of view, were not dangerous; and their stay in hospital was shorter. On the basis of his knowledge of the patient's pre-morbid personality, present way of life and emotional attitude towards one or more relatives after regaining consciousness, it was often not difficult for the doctor to interpret the significance of the suicide attempt. In not a few of these cases, such large aspects of the personality were functioning in dissociation from the conscious life that they were unaware of the element of " domination technique " in their suicide attempts. For most of the patients of this type, in fact, self-extinction as such is not the most important motive, but only one of many possible means of attaining their aims in regard to important persons about them. Schopenhauer's words, " Der Selbstmörder will das Leben und ist bloss mit den Bedingungen unzufrieden, unter denen es ihm geworden " (The suicide desires life and is only discontented with the conditions under which he has obtained it) (14) apply with particular appositeness to these patients.

The frequency of psychopathic-hysteric traits in this group was strikingly high. Often the immediate provocation was a conflict with the spouse or other near relative arising out of an attempt by such person to refuse the patient's unreasonable expectations and demands. Rightly or wrongly, many people feel themselves responsible for what happens to their nearest and dearest. The gesture of attempting suicide can in such circumstances be a very effective expression of " domination technique " which terrifies the intended person into continued surrender. With the patients in question it was often jealousy, a feeling of being wronged and an unconscious desire for revenge that lay behind the attempted suicide. But even if not wholly seriously meant, such attempts nevertheless mean in many instances that the person is toying with death. Generally it can be said that the stresses which the patients have reacted against were frequently not overwhelmingly great; the traits of his personality are the main cause of his difficulties. The trauma which provoked the act was rarely sufficient to explain the reaction. This was essentially conditioned by the patient's personality, only the actual timing being determined by the trauma.

Among the predominantly not seriously intended suicides, there were relatively fewer cases where previous attempts at suicide had made hospitalization necessary though, on the other hand, intimations of suicide threats were often forthcoming during anamnesis. It therefore seems as if attempted suicides of this type are rather in the nature of non-recurring phenomena. Little or no guilt feeling or self-reproach was evident. As a rule there was a serious discrepancy between the patient's knowledge of himself and his behaviour in his personal intercourse with others. The total lack of insight into the primitive character of his own motivation and the tendency to project himself outward made it often difficult to apply psychotherapy. Nor were these patients anxious to undergo psychotherapy. They were not easy to live with, and many conversations with relations revealed that the latter had long since given up the struggle in despair, and become resigned.

The question has been asked how far easy access to barbiturates in many homes has increased the incidence of suicides or attempted suicides. In defence or barbiturates, it has been argued that they also save many human lives. In the first place, they can rid the anxious person of his or her tension, and give the potential suicide a good night's sleep and with it a new courage to live. It is also asserted that many potential suicides take barbiturates as an alternative to a more drastic and more irrevocable self-destruction. As the immediate prog-

nosis of acute cases of barbiturate poisoning is so good, with a mortality of only 3-6%, it should be possible to save many human lives in this way. There may perhaps be something to be said for these arguments in the case of really seriously intended suicidal intoxication, but this applies to only a fraction of cases (about one-third). Furthermore, there are available to us today tranquillizers and antihistamine preparations which can compete with barbiturates in efficacy as sleeping draughts, and have a much broader therapeutic range. *In the majority of predominantly not seriously intended attempts at suicide with barbiturates, we believe that easy access does in fact increase the frequency of intoxication cases requiring hospitalization.* It is characteristic of this type of patient that under an acute emotional reaction in a personal relationship situation he has recourse to the medicine which is accessible as an alternative to other outlets for anger and irritation, as Wiingaard (3) has asserted. We would say that if practising doctors were as prudent in prescribing barbiturates as most psychiatrists are now, a considerable number of suicide attempts of the not seriously intended type could be avoided. They represent a category of patients who in the first few days, at any rate, require continual watching. Practically speaking, all these not really seriously intended cases of attempted suicide are admitted to hospital late in the evening or during the night, and represent an additional problem on that account.

The decrease in mortality in acute cases of barbiturate poisoning from about 20% to about 4% in the course of the last twenty years is striking. But here, as in many other fields, what has been achieved is a development from mortality to morbidity. If, in the future, such patients are not merely to be prevented from dying but also helped to live without relapse, an extension of the psychiatric services for this category of cases is required. What we have said up till now has, in the main, merely given us an opportunity to draw attention to some of the complex problems which arise in this connexion.

Barbiturate Addiction

Particularly in the years immediately following the First World War, a lively discussion went on as to whether barbiturates could produce addiction. The literature available now makes it clear that there is indeed a great danger of addiction through the use of barbiturates (15, 16, 17, 18, 19, 20). This swing in opinion is strikingly brought home by a comparison of the 1940 and the 1954 editions of Goodman & Gilman's textbook of pharmacology (17). In the 1940 edition, not a word is said of barbiturate addiction, chronic poisoning being regarded solely as the cumulative result of the therapeutical use of prolonged-action barbiturates. But the latest edition lays great stress on the danger of addiction from the use of barbiturates, particularly the rapid action types, and categorically states that barbiturate addiction is a far more serious problem than morphine addiction. This change in attitude is primarily due to the conclusive results produced by Isbell and his collaborators (21, 22, 15) at the Lexington hospital.*

Over the years, the concept of " drug addiction " has been variously defined. The WHO Expert Committee on Drugs Liable to Produce Addiction defined it as follows in 1950:**

" Drug addiction is a state of periodic or chronic intoxication, detrimental to the individual and to society, produced by the repeated consumption of a drug (natural or synthetic). Its characteristics include:

" (1) An overpowering desire or need (compulsion) to continue taking the drug and to obtain it by any means;

" (2) A tendency to increase the dose;

" (3) A psychic (psychological) and sometimes a physical dependence on the effects of the drug."

With regard to concepts, a distinction must be drawn between addiction, as defined above, and habituation. In the latter condition, there is no compulsive need of the drug, but only a strong desire for it. Furthermore, there is little or no tendency to increase the dose; dependence on the drug is psychological and not physical, hence there is no abstinence syndrome, and any detrimental effects trouble the individual rather than anyone else.

Our own material takes account only of unmistakable cases of addiction conforming to the criteria laid down by the WHO Expert Committee.

The questions to which we were mainly concerned with finding an answer were the following:

1. How often is drug addiction diagnosed among patients in a medical department with psychiatrists in permanent attendance, and how often is it a case of addiction to barbiturates? How often is addiction to barbiturates found in conjunction with other drug addiction? On what diagnoses were the patients admitted to hospital?

2. What psychiatric diagnoses have such patients had?

3. What is the marital status and working capacity of the patients?

4. What measures did the psychiatrist recommend and what has been done in regard to further treatment for this group of patients?

Methods used

To try to answer these questions we went through the case histories of patients admitted to ward IX at the Ullevål hospital between 1 November 1955 and 31 October 1957, and diagnosed as drug addiction cases.

Results

Incidence

In the two-year period covered by the inquiry, drug addiction was diagnosed in 63 patients in all, and of these 60 (1.6% of total admissions to the ward) were cases of addiction to barbiturates alone or to barbiturates as well as other narcotic substances. The other 3 were cases of abuse of morphine or similar preparations which we can ignore.

Age and Sex Distribution, Marital Status and Fitness for Work

The case material consisted of 20 women and 40 men, 28 being married, 18 single, 7 divorced or separated, and

* See *Bulletin on Narcotics*, vol. IX, No. 2: Abuse of barbiturates, by H. Isbell, M.D.

** See *Bulletin*, vol. IV, No. 3.

TABLE 3

Age and sex distribution of sixty barbiturate addicts

Age group →	Total	Under 20	20-40	40-60	60-70	Over 70
Female	20	1	5	9	3	2
Male	40	0	8	25	5	2

TABLE 4

Employment status of sixty barbiturate addicts

Addicts	Without regular employment	Unfit to work	In work	Pensioned	Housewives
Female	5	3	6	3	3
Male	22	4	12	2	0
TOTAL ...	27	7	18	5	3

7 widowed. Their age distribution is shown in table 3, from which it will be seen that more than half the cases were in the 40-60-year age group. Table 4 shows incapacitation and employment situation. Thirty-four patients, or more than half, had either been without regular employment for years or had more recently become unfit for work. Only 18 of the 60 barbiturate addiction cases were gainfully employed.

Reasons for Admission to Hospital

Of the barbiturate addiction cases, 44 were admitted with a diagnosis of intoxication. In 9 cases, this was attributed to a serious attempt at suicide, in 24 to attempts without any real intention to commit suicide, while 13 cases were assumed to be due to the addicts' having taken an overdose of barbiturates. Of the remaining patients, 2 were admitted for curative treatment. Twenty-three cases had been previously admitted to hospital for poisoning, 16 of them two or more times (2 had been in 12 times before and one 9 times).

The other 14 cases were admitted on other somatic diagnoses.

Duration of Addiction

The approximate duration of abuse of drugs was known in the case of 44 patients; these had indulged in abuse of barbiturates for periods varying from one to 25 years, the *average* being 7.7 years. Other patients admitted to having indulged in such abuse for "some years".

Preparations misused

Forty-three patients engaged in abuse of barbiturates only (in 6 cases Pentymal, 3 cases Allypropymal, 2 cases Fenemal and 1 case barbituric antalgics, the others taking various barbituric preparations). In 17 cases there was evidence of simultaneous abuse of other euphoria-producing substances, mostly morphine, but also amphetamine, bromine and in one case marihuana. Thirty-four of the 60 patients were or had been alcoholics.

In 14 cases barbiturates were the substance to which the patient first became addicted, in 6 cases morphine, and in 33 cases alcohol; in 7 cases the substance taken was unknown.

Barbiturate Concentration in the Serum

The presence of barbiturates in the serum was detected in 37 cases, the average concentration being 4.4 mg/100 ml. In the case of those addicts not admitted on a diagnosis of intoxication, the average concentration was 3.4 mg/100 ml. The highest concentration was 30.5 mg/100 ml in a patient who was admitted for intoxication and died. In 2 cases, only traces of barbiturates were found and in 2 cases the test result was negative. In 19 other cases the concentration was not measured, mainly because the intoxication was slight and the patient was soon discharged.

Psychiatric Diagnoses

Of the 60 barbiturate addicts, 54 in all were given a psychiatric examination. The personality diagnoses for those examined are set out in table 5. In all cases the reaction diagnosis was

TABLE 5

Personality diagnoses of fifty-four addicts subjected to psychiatric examination

Addicts	Number
Persons lacking in self-control	16
Unbalanced psychopaths	9
Persons having no apparent abnormalities	6
Psycho-infantile (hysteriform) persons	6
Persons suffering from organic brain disease	5
Hysteriform psychopathic persons	3
Hyper-sensitive persons	3
Persons having other forms of psychopathy	3
Feeble-minded persons	2
Debilitated (asthenic) persons	1

drug addiction, and in 47 cases there was an additional reaction diagnosis. In 34 cases (8 women and 26 men), the additional diagnosis was chronic alcoholism. Ten patients (5 women and 5 men) were found to be neurotic, 6 of them having depressive neurosis, 2 giving a neurotic insufficiency reaction, one having angst neurosis and one suffering from neurasthenia. Three of the patients were psychotics, 2 of them with delirium.

The situation which led them to become addicts (situation diagnosis) is unknown in most cases, but 15 patients (8 out of 20 women, 7 out of 40 men) were brought to it through prolonged use of narcotic drugs medically prescribed for an illness. Ten of them had a definite somatic condition, the other 5 disorders of mainly functional origin.

Thirty-three of the patients had previously been admitted to a psychiatric ward.

Therapy

The average number of days in hospital for barbiturate addicts was 10.8, the actual number varying from one to 100 days. Twenty patients were in the ward 3 days or less.

They were treated with heavy doses of vitamins B and C, often in combination with small doses of insulin (3 plus 2 nordic units a day). Some of the patients also received tranquillizers, in the form of chlorpromazine, reserpine or meprobamate. For agitation during the first few days reserpine — e.g., in intramuscular injection of 2.5 mg 2 to 3 times a

day — can safely be given. Reserpine has no intensifying effect worth mentioning on alcoholic or barbiturate intoxication, and the intensifying effect of chlorpromazine presents no danger factor from the practical clinical standpoint. Eighteen patients were given barbiturates or other narcotic drugs in the ward. In no case was any patient given the full addict treatment with isolation and ban on visits. Thirteen of the patients examined by psychiatrists were transferred to the psychiatric ward. Eleven others were offered a transfer to the ward but declined. Of the remainder, 9 were removed to other institutions (nursing homes, convalescent homes or institutions).

Eleven of the patients were readmitted to hospital on grounds of the same drug addiction during their observation period, which averaged a year.

Are Barbiturate Addicts a Little-known Public Health Problem?

As our case material on barbiturate intoxication shows, no less than 44 of the 117 patients with barbiturate poisoning were drugs addicts — i.e., about 40 per cent, which is a surprisingly high proportion. There were a further 14 patients who had been admitted to the ward on the strength of other diagnoses and were classified as addicts during their stay.

The frequency of admission of addicts to a medical ward is no pointer to the incidence of such conditions amongst the population. There is scarcely any morbid condition where the disproportion between the number of patients and the number seeking treatment in hospital is so marked as in drug addiction. A genuine resolve to put an end to the abuse is very seldom found, and even among these cases not all are willing to be admitted to hospital because of the discriminatory treatment they assume they will receive from doctors and hospital staff. Furthermore, the vast majority of those who either decide of their own accord to enter hospital, or are in such a state of exhaustion that their relatives take action, are admitted to the psychiatric ward. Over half our patients were either without regular employment or unfit to work.

All these circumstances considered, the figure of sixty in the course of a two-year period must be said to be high for an internal medical department, where a considerable number of urgent cases are received.

Even though the material we have is limited, it does bring out one fact — namely, the frequency of barbiturate addiction. The material includes all cases of drug addiction admitted during a period of two years. All but three cases displayed a dependence on barbiturates either by themselves or in conjunction with other narcotic drugs. Thus, from the material we have, it seems that we must support Goodman & Gilman's claim that addiction to barbiturates is a more serious problem than morphine addiction.

Can any conclusions be drawn from our material regarding the presence of common traits in the personality structure of the addicts? Comparison of the personality diagnoses for cases of acute poisoning with those of the addict group shows that a psycho-infantile personality is less frequent among the addicts. The majority of the addicts are described as unstable or psychopathic and there are many cases of cerebral damage or feeble-mindedness among them. There were relatively few who had not previously had something odd about them. Most of these patients seem to have been already suffering from a radical personality defect. Attention must, however, be drawn to the great difficulty of forming an opinion on the premorbid personality structure of such patients when their personality has often been greatly altered through prolonged abuse of drugs.

Our experience tends to show that there is no specific type of personality which has a predilection for a particular drug. There seems rather to be a general addiction or, perhaps better, a craving for euphoria, it being more or less a matter of chance whether the substance that happens to be used for the purpose is alcohol, barbiturates or morphine preparations. In very many cases a combination of several substances is used. The super-ego, the inhibiting and controlling faculty of our personality, has been facetiously described as "that part of the psyche which is soluble in alcohol". An unimpaired cerebral cortex may be taken as an essential condition for the proper functioning of that faculty. Barbiturates and morphine may also be presumed to affect the faculty in the same way. Möller (23) defines intoxication in general as a state in which the function of the brain proper is more or less diminished. Positive mental euphoria, which the addict cannot resist the temptation to enjoy, consists in all probability in a release from inhibitions. The material in our possession sheds very scant light on any external factors which might be decisive in regard to drug addiction. The information obtained from the addict himself rarely corresponds to the true state of affairs. The addict is often convinced that his abuse of drugs is due to an undeserved stroke of fate that has befallen him, and musters up considerable resistance to the explanation that is often as plain as a pikestaff to his close associates, that it is primarily tendencies and a craving within him that have led him to intoxicate himself instead of facing up to external difficulties. Half of our patients have at some time been admitted to a psychiatric clinic, on an average about four times each. Their case histories and observations based on them point to the conclusion that addiction is to be regarded as only one of many manifestations of a deep-seated personality defect, but dependence on narcotic drugs represents a malignant complication of the basic psychiatric disorder. This complication is in itself difficult to overcome, and makes it pointless to achieve a successful treatment for the basic disorder. By helping to turn a neurotic into a drug addict, a physician who prescribes barbiturates can easily ruin the patient's chances of cure by radical psychotherapy. This fundamental problem is best brought out by the following remarks by Kubie: "They (the Russian physiologists of the Pavlov school) demonstrated that it is only in a state of craving that important new connections can form in the central nervous system. The psychoanalytic version of this fact is Freud's observation that an analysis makes best progress in the presence of deprivation."

The material compiled by us shows no preponderance of persons in occupations connected with the production, distribution or prescription of medicines. This may be because the material is not representative, but it may also be that the

circumstances are different when addiction is due to barbiturates and when it is due to morphine. Anchersen (25) found in his material on morphine addiction that roughly one-third of the victims were connected with occupations giving easy access to morphine. The fact that it is not so hard to lay hands on barbiturates as on morphine probably explains why the difference in frequency of "unexposed" and "exposed" occupations is not so great in the case of barbiturate addiction, the position being more similar to that found in the case of alcohol.

Anchersen also found from his data on morphine addicts that a good half of those admitted to psychiatric clinics between the years 1928 and 1942 has shown clear signs of psychopathic disorder before. In our case material, too, psychopathic disorder is very frequent. In relatively few cases is neurosis or endogenic disturbance at the root of the drug addiction. In such cases the reason for abuse of drugs can be said to be a longing to return to a lost state of normality. The great majority of addicts, to begin with, take their drugs rather to achieve something than to escape something. As the contemporary French author and member of the Academy, Jean Cocteau, puts it: "Trying to persuade a drug addict to give up his poison is like urging Tristan to slay his Isolde on the plea that he will feel so much better afterwards." (26) But, quite apart from the addict's pleasurable experience and from the complex of personality defects and the circumstances of his life which led to his abuse of drugs, fear of the abstinence syndrome helps to make him continue such abuse. The emotional immaturity which is at the root of many cases of drug addiction often reveals itself in the patient's life story. In other matters, too, he will have shown little ability to forgo immediate satisfaction or make present sacrifices for the sake of a more distant goal.

With our case-material it was impossible to obtain any reliable information either from the patients or their relatives on the amounts of barbiturates consumed. According to the findings of Isbell (15), it can be assumed that a barbiturate addict absorbs on an average 0.8 gr of the substance per day. Apparently the dose must be in the neighbourhood of this amount for a clear case of addiction to develop. It is a known fact that there are persons who for years have taken 0.10 or 0.20 gr of barbiturates daily in order to get a good night's sleep with no noticeable ill-effects. That does not alter the fact that certain individuals — it is not easy to say which beforehand — gradually develop barbiturate addiction in such circumstances. With habituation the sleep-inducing power of the drug declines, the dose has to be increased, and the effect of the barbiturates changes, inducing, instead of sleep, a state of mental well-being, which the patient feels as a cheerful mood, but which more often strikes his relatives as passiveness and loss of critical sense. When barbiturates are taken in much larger doses than prescribed by a doctor and during the day, they are no longer a soporific, but an intoxicant. Our material shows that even many alcoholics are tempted to change over to that "intoxication which does not stay on the breath". It is a well-known fact that abuse of barbiturates is one of the most common and serious complications of chronic alcoholism.

There are, however, quite definite cases where the craving has been induced in relatively normal persons who previously had never felt an unusually strong need for euphoria but have been given analgesics or cough cures for troublesome physical ailments over a long period. It is to be hoped that the pharmaceutical industry will ultimately produce specific analgesics, anti-tussives, sedatives and astringents that do not have the troublesome secondary effect of inducing euphoria. For in all cases, with the possible exception of amphetamine, the euphoria-inducing property of the drugs in question is not an indispensable feature that has to be accepted in order to obtain the desired symptomatic effect. Morphine and similar preparations are intended to have an analgesic, anti-tussive or astringent effect, barbiturates are designed to induce sleep or calm in acute anxiety disorders. The development in recent years of various tranquillizers and specific anti-tussives generally without inhibitory effects on the central nervous system holds out the hope that the risk of drug addiction can be successfully reduced. Experiments over a long period with tranquillizers in the treatment of drug addicts have proved disappointing. Though they dispose of the abstinence symptoms during the withdrawal stage, after discharge the addict is not satisfied with the relaxed feeling they give, but demands the euphoria brought on by the effect of the drug in dulling the consciousness. More often than not the patients slide back into their old abuse, thereby revealing their true nature as euphoria seekers.

The fact that so few serious abstinence symptoms were found in our case material is due to a variety of factors. One is that eighteen of the patients were given barbiturates or other narcotic drugs in the ward, another that some of the patients are transferred to the psychiatric wards relatively soon after their admission. Again, most of our patients are admitted to the ward on the grounds of barbiturate intoxication and therefore have an accumulation of barbiturate in their system, which is subsequently eliminated. Finally, many demanded during their first few days in hospital to be discharged and continue their abuse of the drug. Of the three cases of psychosis, two were abstinence psychoses.

As our findings show, the opportunities for treating the addicts were limited. It may be generally said that it is difficult to carry out treatment for drug addiction in a medical department. There, the most important thing is to treat the patient's somatic symptoms and work on his mental state so as to persuade him to undergo in-patient treatment over a long period in a psychiatric institution. There is no way of treating addicts who do not wish to be treated, since at present a patient cannot be ordered to enter an institution. This is a grave deficiency where the treatment of drug addicts is concerned. From the epidemiological standpoint if from no other, the position is an unfortunate one, since many addicts, especially the socially depraved, constitute foci for the propagation of the disorder.

The prognosis for a lasting cure for firmly established drug addiction is bad. So long as there are still no special clinics for addicts, we have to try to get them into a psychiatric observation ward and then induce them where necessary to

go voluntarily into a home. It is the private medical practitioner's duty to try and persuade his patient to accept treatment. By adopting a more severe attitude towards the addict in the matter of prescribing barbiturates, he can put pressure on him to submit to treatment.

The prognosis being so bad, proportionately more weight must be laid on prophylaxis. The importance of restrictive prescribing of barbiturates, as a long-term prophylactic measure, is not to be underestimated.

In a ward with 175 beds, 30 barbiturate addicts are admitted per year. In Oslo there are about 1,300 medical ward beds in hospitals with regular medical staff. As it may reasonably be assumed that the incidence of drug addicts in the other medical wards is about the same, probably 240 barbiturate addicts are admitted to medical wards in Oslo in the course of a year. To these must be added the barbiturate addicts in private medical nursing homes without regular medical staff. Since, as already pointed out, the figure of thirty we have given is a minimum, we may take it that the extent of the problem for all medical wards together is more or less as stated. The other specialist departments presumably have their drug addiction problems too, but probably to a lesser degree. For withdrawal treatment patients are practically without exception admitted to psychiatric wards, and those of the Oslo Municipal Hospital, where the vast majority of such patients in Oslo are undoubtedly to be found, admit about 120 barbiturate addicts per year. Thus, at a conservative estimate, in the city of Oslo with a population of 400,000, one barbiturate addict is admitted per day to a hospital medical department.

These considerations would suggest that barbiturate addiction is a far greater problem than it was hitherto thought to be in this country. The Ministry of Health is constantly receiving reports on cases of drug addiction from doctors, pharmacists, and the relatives of addicts. Apart from these reported cases, there are also registered addicts who are discovered through the regular auditing of narcotic drug registers in pharmacies. The Ministry of Health keeps a list of addicts, but it does not include those patients who have agreed to enter a hospital as in-patients for withdrawal and curative treatment.

The addicts reported to the Ministry of Health during the eight-year period from 1950 are shown in table 6, classified according to sex and type of addiction. It will be seen that of 231 drug addicts registered with the Ministry of Health in the eight-year period 1950-1958, only 65 — i.e., about 30 per cent — indulged in abuse of barbiturates alone or in combination with other drugs.

The low figure for reported cases of barbiturate addiction can probably be attributed in part to the fact that many doctors and pharmacists have not hitherto looked upon dependence on barbiturates as a form of drug addiction. Barbiturates have also been relatively easier to obtain than other drugs, and abuse is therefore more difficult to detect. A further reason why so many cases of barbiturate addiction remain unknown may be that barbiturate addicts do not suffer from malnutrition so often as morphine addicts.

TABLE 6

Drug addicts registered with the Ministry of Health in the eight years 1950-1958, analysed by sex and drugs used

Drug	Male	Female	Total
Combination of several opiates or morphine-like preparations	27	28	55
Morphine (and/or Thebaine)	25	18	43
Opium	3	8	11
Hydromorphone (Dilaudid)	1	1	2
Hydrocodone (Dicodid, Nyodid)	18	3	21
Phenatyl	1	0	1
Codeine	0	1	1
Pethidine (Dolantin)	1	4	5
Methadone (Amidone)	1	7	8
Ketobemidone (Ketogan, Cliradon)	3	0	3
Amphetamine	10	5	15
Aphatin	1	0	1
Barbiturates	15	11	26
Combination of barbiturates and other preparations	27	12	39
TOTAL ...	133	98	231

OFFICIAL STEPS TAKEN IN NORWAY TO KEEP DOWN THE ABUSE OF DRUGS

Despite the relatively low official figures, the public health authorities have been aware that abuse of narcotic drugs is a serious social and medical problem in this country, and have enacted new legal measures to cope with it.

The right of medical practitioners to prescribe drugs with a narcotic effect is restricted under the royal decree of 27 September 1957. This stipulates that prescriptions for a whole series of medicines which are set out specifically cannot be repeated. Quantities must be stated in figures and words. Pharmacists are legally bound to retain the prescriptions and keep them for three years, and to hand them over to the public health authorities if so requested (cf. Medical Practitioners' Rights and Duties Act, quoted below). The substances covered are amphetamine, dexamphetamine, diacetylmorphine, dihydrocodeine, hydrocodone, hydromorphine, ketobemidone, cocaine, methadone, morphine, oxycodone, opium, pethidine and tetrapon.

Restrictions have also been placed on barbituric acid derivatives by the following provision:

"In order to be valid an endorsement permitting the repeated dispensing on the same prescription of a medicine whose sole or chief constituent is a barbituric acid derivative or like substance which may offer temptation to abuse must contain an indication of the minimum time that must elapse between each dispensing — e.g., 'Rep. III times — ter — 3 weeks' interval'."

The Act of 29 June 1957, supplementing the Medical Practioners' Rights and Duties Act of 27 April 1927, as amended by the Act of 19 June 1936, contains special provisions designed to prevent misuse of the rights to prescribe narcotic substances. The following are some of its provisions:

Article 5.[1] Subject to any restrictions laid down by law or in regulations issued under the law, every medical practitioner has the right to prescribe such medicines as are necessary for the exercise of his profession. However, by making a declaration to the Ministry, he may for a specified period renounce the right to prescribe all narcotic drugs or certain groups of such drugs.

Subject to the limitations arising from professional secrecy, the Crown shall issue general provisions on the wording of prescriptions and may, after consulting the Faculty of Medicine and the Medical Board, determine that prescriptions for specially designated drugs shall be kept in pharmacies for inspection by the appropriate control authority. The production of such prescriptions as evidence may be demanded in criminal cases or when action is taken to deprive a medical practitioner of the right to exercise his profession or hold the post of a medical officer of health, or when cases are brought before the Supervisory Council for the Prescription of Narcotic Drugs.

Article 5a.[1] Where there are reasonable grounds for assuming that the prescription of narcotic drugs by a medical practitioner may be regarded as an unjustifiable medical activity, the Ministry shall warn him, and, if the warning is not heeded, shall bring the matter before the Supervisory Council for the Prescription of Narcotic Drugs.

The Ministry may from the time when the case is submitted to the Council, deprive the medical practitioner of the right to prescribe narcotic drugs until a final decision has been taken on the case.

Article 5b.[1] If the Council finds the medical practitioner has prescribed in an irresponsible manner, it may deprive him for a specified period not exceeding five years of the right to prescribe all or certain groups of narcotic drugs.

Before taking such decision, the Council shall give the practitioner a hearing and acquaint him with the documents and other information relating to the case.

The Council may restore to the medical practitioner at his request the right to prescribe narcotic drugs before the expiry of the time fixed.

Article 5c.[1] 1. The Supervisory Council for the Prescription of Narcotic Drugs shall consist of a chairman, a deputy chairman and two other members who, with their alternates, shall be nominated by the Crown.

The chairman and deputy chairman shall possess the qualifications of judges of the High Court. The two other members shall be experienced medical practitioners.

2. No decision of the Council shall be valid unless all the members are present.

3. The decision to withdraw from a medical practitioner the right to prescribe narcotic drugs must be unanimous.

Similarly, the decision to restore that right to a medical practitioner before the expiry of the time fixed must be unanimous.

4. The Council shall give reasons for its decisions.

5. The regulations concerning disqualification in the law of 13 August 1915, concerning tribunals, article 106, 1 to 4, and article 108, shall apply, *mutatis mutandis*, to the Council.

6. The members shall be entitled to remuneration for their meetings and to travel and subsistance allowance in accordance with regulations to be laid down by the Department.

7 The Crown may issue more detailed regulations concerning the composition, working-time and procedure of the Council.

Article 5d.[1] Where in virtue of the preceding provisions a medical practitioner has lost wholly or in part the right to prescribe narcotic drugs, the drugs necessary for his practice shall be prescribed by the competent medical officer. However, in individual cases, the Ministry may authorize another medical practitioner willing to do so, to write out such prescriptions.

The Crown may lay down more detailed regulations concerning such prescriptions.

Article 5e.[1] Any medical practitioner shall, without prejudice to the rules of professional secrecy, if required by the Ministry, provide information necessary for any inquiry into eventual abuse of narcotic drugs.

Article 5f.[1] The Crown shall determine which drugs are to be regarded as narcotic drugs for the purpose of the provisions of this law.

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20. Any person contravening the provisions of this law, or regulations issued in virtue thereof, shall be liable to a fine or to imprisonment not exceeding three months unless a more severe penalty for such contravention is laid down in the general criminal code. A medical practitioner who prescribes narcotic drugs after he has voluntarily relinquished his rights under article 5, or has been deprived of the rights under article 5a, paragraph 2, or article 5b, shall be liable to the same penalty.

The legal authority for treating drug addicts in Norway is to be found in the Act of 26 February 1932 on temperance boards and the treatment of inebriates, together with the supplementary Act of 6 July 1957. The latter Act, which applies the provisions of the earlier Act to drug addicts as well, was adopted but not put into effect because of the lack of facilities for placing drug addicts in institutions.

The Act provides for the establishment in each commune of a democratically elected temperance board consisting of not less than three members of the municipal council, its tasks being partly preventive and partly administrative. Thus, the board shall make proper arrangements for alcoholics or drug addicts if so requested by the patient himself, his next of kin or any of a number of clearly specified public authorities.

If such person refuses to comply with the board's order or if the Board deems it otherwise necessary, it may under its regulations and without regard to his own wishes in the matter, order him to be committed to an approved institution

[1] Law of 28 June 1957.

for treatment for up to two years when, through abuse of alcohol or narcotic substances, the said person:

1. Maltreats his spouse or children or exposes his children to moral danger or neglect;

2. Fails to fulfil his maintenance obligations under the law;

3. Exposes himself to serious bodily or mental harm, endangers his own life or that of others, or repeatedly makes himself a public nuisance;

4. Becomes a burden on public assistance or on his family;

5. Dissipates or gambles away his worldly goods to such an extent that he or his dependants may become indigent.

When a decision involving deprivation of freedom has to be taken, the board's proceedings shall be presided over by the district or local magistrate.

The person concerned shall be summoned to a hearing and shall have the right to be assisted by a lawyer or by another representative acceptable to the board's chairman.

If it sees occasion to do so, the board shall, without resorting to compulsory commitment to an institution, try to have the addict cured of his habit. It shall also apply a series of practical measures, which are specified in detail, to help the drug addict and his family.

Summary

The experience of psychiatric clinical wards in Norway suggests that 75% of the drug addicts are using barbiturates.

At present, a thorough psychiatric examination with corroborative information from other sources constitutes our most reliable case-finding method as far as drug addiction is concerned. It is difficult to detect the drug addicts in a typical population group. Over a two-year period in an internal medicine department with regular staff psychiatrists, all patients giving grounds for suspicion of drug addiction were given a psychiatric examination. A very large number of drug addicts were found among patients admitted after attempting suicide with barbiturates; hence all such patients were subjected to systematic psychiatric examination.

Of a series of 207 cases of acute intoxication, 137 (81 women and 56 men) were cases of barbiturate intoxication. In 37 cases, alcohol poisoning was diagnosed at the same time. Of the 117 patients subjected to psychiatric examination, abuse of barbiturates was found in 44 cases. In 90 cases, suicidal intentions were taken to be the reason for the intoxication, 26 being genuine cases of abortive suicide, the other 64 having no real intention of taking their own lives. Erotic conflict or family trouble was the commonest cause of attempted suicide. The most usual type of personality was the psycho-infantile type, particularly among the cases of not really serious attempts at suicide.

A "paradoxical barbiturate effect" was found in three elderly patients who developed symptoms of derangement after therapeutic doses.

Among the 3,750 patients admitted during the two-year period, 63 were drug addicts, 60 of them being addicted either to barbiturates alone or to barbiturates in conjunction with other narcotic drugs. Forty-four of the patients were admitted to hospital with acute intoxication, and more than half of them were also suffering from chronic alcoholism. In 15 patients ("medical addicts") addiction had developed after prolonged treatment with narcotic drugs prescribed by a physician for various complaints. In the other cases ("social addicts") the main cause of addiction was taken to be a personality defect with social maladjustment. More than half were out of work, and on an average addiction was of 7.7 years' standing. Over half had previously been treated in a psychiatric institution.

The prognosis in the case of well-established drug addiction is bad; hence the main emphasis must be placed on prophylaxis. The importance of restricting the prescribing of barbiturates, as a long-term prophylactic measure, is not to be underestimated. Most Norwegian psychiatrists nowadays are agreed that any use of barbiturates as a daytime sedative is contra-indicated in treating nervous states. The administration of barbiturates can be viewed without misgiving only for occasional insomnia in persons with no apparent psychological abnormalities. Most Norwegian psychiatrists refrain from prescribing barbiturates at all, and do not feel the loss of them.

In conclusion, reference is made to the measures put into force by the Norwegian health authorities to combat the spread of drug addiction. Mention is made of the legal basis for compulsory commitment of drug addicts to institutions. One of the main problems in that connexion is that of appropriate restrictions to prevent the uncritical prescribing of narcotic drugs. A new Act now makes it possible in Norway by administrative action to deprive a medical practitioner of his right to prescribe narcotics without depriving him of his licence to practise.

Even though drug addiction must be regarded as a symptom and complication of a more deep-seated psychiatric disorder, it is of great importance from the standpoint of mental hygiene to combat dependence on drugs. A secondary drug addiction renders impossible both spontaneous recovery and the application of psychotherapy to the fundamental personality disorder.

It is to be hoped that the new tranquillizers will lead to fewer psychiatric patients' falling victims to barbiturates in future.

References

1. Editorial: Lancet, I: 293, 1956.
2. LINGJÆRDE, P. & RÖMCKE, C., *Tidsskr. for den norske Laegefor.*, *75*: 1, 1955.
3. WIINGAARD, P., *Ugeskrift for Laeger*, *111*: 346, 1949.
4. DAHLGREN, K. G., *On suicide and attempted suicide*. Lund, 1945.
5. KRANE, B., *Tidsskr. for den norske Laegefor.*, *69*: 290, 1949.
6. ETTLINGER, R. W., FLORDH, P., Attempted suicide. *Acta Psych. & Neurol. Scand.*, Suppl. 103 : 1955.
7. LOUS, P., *Acta pharm. & toxicol.*, *10*, 134, 1954.
8. RICHARDS, R. A., *British Med. Journ.*, I : 331, 1934.
9. AAMODT, T., *Tidsskr. for den norske Laegerfor.*, *76* : 606, 1956.
10. GAUSTAD, V., *Ibid.*, *74*: 743, 1954.

11. BOREUS & SANDBERG, *Acta Physiol. Scand., 28:* 6, 1953.
12. BOREUS & SANDBERG, *Ibid., 28:* 266, 1953.
13. LEVINE, M., *Psykoterapi i medisinsk praktik.*, Natur och Kultur, Stockholm, 1946.
14. SCHOPENHAUER, A., *Die Welt als Wille und Vorstellung*, I. : Verlag von Philip Reclam jun. Leipzig.
15. ISBELL, H., ALTSCHUL, S., KNORNETSKY, C. H., EISENMANN, FLANARY, H. G. & FRASER, H. F., *Arch. Neurol. & Psychiatr., 64:* 1, 1950.
16. Symposium on Drug Addiction, *Am. Journ. Med., 14:* 537, 1953.
17. GOODMAN, L. S. & GILMAN, A., *The Pharmacological Basis of Therapeutics*, The MacMillan Company, New York, 1956.
18. ANCHERSEN, P., *Tidsskr. for den norske Laegefor., 72:* 129, 1952.
19. ANCHERSEN, P., *Ibid., 72:* 303, 1952.
20. ANCHERSEN, P., *Ibid., 76:* 979, 1956.
21. KONNETSKY, C. H., *A.M.A. Arch. Neurol. & Psychiat., 65:* 557 1951.
22. HILL, H. E. & BELLEVILLE, R. E., *Ibid., 70:* 180, 1953.
23. MÖLLER, K. O., *Stimulanser*, Gyldendal Norsk Forlag. 1947.
24. KUBIE, I. S., *Practical and theoretical aspects of Psycho-analysis*, International Universities Press, Inc., New York, 1950.
25. ANCHERSEN, P., *Acta psychiatr. & Neurol., 22:* 153, 1947.
26. COCTEAU, J., cit. K. O. Möller (23).

Note

Present state of the struggle against the abuse of opium in Iran[1]

In the three years which have followed the enactment of the law of 1955 prohibiting the cultivation of the opium poppy and the use of opium in Iran, results have been obtained in both the reduction of cultivation and the struggle against opium addiction, as follows:

One thousand four hundred and ten hectares (about 3,000 acres) of poppy cultivation have been converted to other crops; more than 120,000 opium addicts have been cured in government establishments; 3,651 opium dens have been closed; more than 4½ tons of opium and opiates have been seized; about 9,000 cases of contravention of the law have been referred to the courts; more than 2,000 individuals have been condemned to prison terms.

According to the estimates of the mission of the Food and Agriculture Organization, the loss of income resulting from the prohibition of opium production is approximately US $30 million. To that sum should be added the expenses incurred in the execution of the law, and the losses incurred by the people who made a living by the trade in opium. This loss has been estimated at about $60 million; it can, however, be considered negligible in comparison with the damage done to public health and the general prosperity by opium addiction, especially since, according to medico-social studies made by Dr. A. Azarakhsh, Director-General of the Iranian Narcotics Control Administration, 87% of all addicts are in the 20-50 age group — that is, the active period o human life.

As a result of the shortage of narcotics supplies for addicts brought about by the Iranian policy of prohibition, the prices of the drugs have sharply risen on the illicit market. While, before prohibition, addicts could obtain a gramme of opium for about $0.02-0.03, they must now pay $1 for a gramme of opium, and $7 for a gramme of morphine on the illicit market. It can be assumed that these prices will tend to increase as the governmental measures become even more effective.

The Ministry of Public Health has lately prepared a bill for Parliament which, in respect of opium, will strengthen the measures by the 1955 law, and deals with all narcotic drugs. This bill provides for very heavy penalties for illicit manufacturers of or traffickers in narcotics, including the death penalty in case of large-scale traffickers.

Iran's experience has shown that in order to succeed in the struggle against the opium evil, quick and comprehensive measures are needed: in the words of the French publicist, Emile de Girardin, "Ineffectual rigour is the worst of all policies; it is like a gun which instead of killing the quarry explodes in the hand of the hunter."

In view of the increased risk of illicit foreign supplies of opium, Iran is counting on international assistance and particularly on that of its neighbours. Some technical assistance has already been given to Iran within the framework of the Technical Assistance Programme of the United Nations and the specialized agencies, and it is hoped that this assistance will be extended.

[1] The present note is a short summary of information furnished by Dr. A. Azarakhsh at the international seminar on narcotic drugs organized by the ICPO in Paris during the spring of 1959. For accounts of the action taken by Iran in suppressing opium production, see *Bulletin on Narcotics*, vol. VIII, No. 3; vol. X, No. 2; and vol. XI, No. 1.

Bibliography

SCIENTIFIC PUBLICATIONS ON NARCOTIC DRUGS IN 1958

Introduction

The following bibliography has been prepared by the secretariat, and includes scientific publications on narcotic drugs which appeared during 1958, as well as a few which appeared earlier but could not, for various technical reasons, be included in the preceding lists published in the *Bulletin on Narcotics*. This bibliography makes no claim to be complete, and information regarding books or articles not included in it would be gratefully received by the Division of Narcotic Drugs, European Office of the United Nations, Geneva, Switzerland.

The bibliography has been arranged by subject in the following way:

Part I. General works

Part II. Opium poppy, opium and drugs manufactured therefrom

- A. Opium poppy, opium and opium alkaloids collectively considered
- B. Morphine
- C. Other phenanthrene alkaloids and derivatives of opium
- D. Other drugs and substances derived from the opium poppy

Part III. The coca leaf and cocaine

Part IV. Cannabis and its derivatives

Part V. Synthetic drugs

- A. General works
- B. Pethidine and related compounds
- C. Methadone and related compounds
- D. Morphinan and morphine synthesis

Part VI. Addiction to narcotic drugs

Part VII. Miscellaneous

Under each heading, publications are arranged alphabetically by author. Owing to the nature of the sources available to the secretariat for preparing this bibliography, several titles are given in translation only. They are preceded by an asterisk.

The bibliography is prepared for both English and French editions; therefore translations in both languages follow those titles which are not in one of the working languages.

Part I. — GENERAL WORKS — GÉNÉRALITÉS

A

ANONYMOUS — ANONYME : The duties of doctors and dentists under the dangerous drugs law and regulations. *Cyprus medical Journal*, 1957, *9:* 11-12, pp. 215-225

ANONYMOUS — ANONYME : Analgesic drugs VII. Narcotics I. *New England Journal of Medicine*, 1957, *257:* 20, pp. 985-987; Analgesic drugs VIII, Narcotics II, *ibid.*, *257:* 24, pp. 1182-1184

ANONYMOUS — ANONYME : Overdosage with analgetics. *New York State Journal of Medicine*, 1957, *57:* 19, pp. 3187-3188

ANONYMOUS — ANONYME : Global fight against illicit drug traffic. *United Nations Review*, 1958, *5*, pp. 22-24

ANONYMOUS — ANONYME: Kampen mot den illegala narkotikahandeln (The fight against narcotics illicit traffic. La lutte contre le trafic illicite des stupéfiants). *Världshorizont*, 1958, *12*, pp. 6-8

ARCHAMBAULT, G. F.; DODDS, A. W. : The handling of narcotics in federal state, county and city hospitals. *Hospital Management*, 1958, *85:* 3, p. 120; passim

ARDEMAGNI, M. : Alcune acquisizioni nel campo degli analgesici (New acquisitions in the analgesic field. Nouvelles drogues dans le domaine des analgésiques). *Bollettino chimico farmaceutico*, 1958, *97:* 4, pp. 233-239

*ARZAMASCEV, A. P. : (La colorimétrie utilisée dans les analyses d'alcaloïdes) (Use of colorimetry in alkaloid analysis). *Aptechnoe Delo*, 1957, *6:* 4, pp. 73-81

ASBROCK, K. H. : Rauschgiftdelikte (Offences connected with narcotics in Federal Germany. Délits relatifs aux stupéfiants en Allemagne fédérale). *Kriminalistik*, 1958, *12:* 1, pp. 19-20

AVI-DOR, Y.; TRAUB, A.; MAGER, J. : Differences in the sensitivity of the DPNH-oxidase system of mitochondrial and sarcosomal preparations to inhibition by narcotics. *Bulletin of the Research Council of Israel*, section A, 1957, *6* A : 3-4, pp. 321-322

B

BECKMAN, H. : *Drugs. Their nature, action and use*. 1958, W. B. Saunders Co., Philadelphia and London, 728 pp. (xvii), ill.

BERTSCHINGER, J. P. : L'OMS et les stupéfiants. *Journal suisse de pharmacie*, 1958, *96:* 19, pp. 377-379

BELL, R. G. : Problems resulting from the use of habituating drugs in industry IV. The problem within industry. *American Journal of Public Health*, 1958, *48:* 5, pp. 585-589

BLECHSCHMIDT, W.; SCHOETENSACK, W. : Der Einfluss von Analeptica auf den Kreislauf der narkotisierten und nicht narkotisierten Katze (Action of analeptics on anaesthetized and non anaesthetized cats. L'influence des analeptiques sur la circulation du Chat anesthésié et non anesthésié). *N.-S. Archiv für experimentelle Pathologie und Pharmakologie*, 1957, *232:* 1, pp. 328-331

C

COHEN, Y. : L'emploi des isotopes en pharmacologie. *Thérapie*, 1957, *12:* 5, pp. 708-36

COLLOM, A. B. : Tears of the poppy; a review of the history of opium. *Journal of the Kansas Medical Society*, 1957, *58:* 9, p. 614; passim.

CUNNINGHAM, D. J.; BENSON, W. M.; HARDY, J. D. : Modification of the thermal radiation method for assessing antinociceptive activity in the rat. *Journal of Applied Physiology*, 1957, *11:* 3, pp. 459-464

D

DAVID, N. A. : Progress in the search for morphine substitutes. *Portland Clinic Bulletin*, 1957, *11:* 2, pp. 33-42

DE BELLA, G. : Nuova metodologia per la determinazione nel coniglio del potere analgesico dei farmaci (New methodology for the

determination in the rabbit of the analgesic power of drugs. Méthodes nouvelles pour déterminer chez le lapin le pouvoir analgésique des drogues). *Bollettino della società italiana di Biologia sperimentale* 1957, *33:* 8-9, pp. 1245-1249

DEBRIS, P. : Les analgésiques non opiacés, *Vie médicale*, 1958, *39*, p. 37; passim

DÖRING, H. J.; GERLACH, E. : Säurelösliche Phosphor-Verbindungen des Gehirns unter dem Einfluss von Anoxie, Ischämie und narkotischen Stoffen (Phosphorate derivatives soluble in acid of brain under influence of anoxia, ischemia and narcotics. Dérivés phosphorés du cerveau solubles dans les acides sous l'influence de l'anoxie, de l'ischémie et des narcotiques). *Archiv für experimentelle Pathologie und Pharmakologie*, 1957, *232:* 1, pp. 271-273

E

ECKENHOFF, J. E.; HELRICH, M. : The effect of narcotics, thiopenthal and nitrous oxide upon respiration and respiratory response to hypercapnia. *Anesthesiology*, 1958, *19:* 2, pp. 240-253

F

FEBVRE, P. : La réaction de Vitali peut-elle devenir une réaction quantitative? *Annales pharmaceutiques françaises*, 1957, *15:* 118, pp. 635-637

FOULK, W. T.; FLEISCHER, G. A. : Effect of opiates on the activity of serum transaminase. *Proceedings of the Staff Meetings of the Mayo Clinic*, 1957, *32:* 16, p. 405

FRASER, H. F. : Problems resulting from the use of habituating drugs in industry. I. Pharmacology of habituating drugs. *American Journal of Public Health*, 1958, *48:* 5, pp. 561-570

FRIEDBERG, V.; RÜBENACH, I. : Untersuchungen über die Nierenfunktion während der Narkose und Operation (Research in kidney functions during anaesthesia and surgical operation. Recherches sur le fonctionnement rénal au cours de l'anesthésie et de l'intervention chirurgicale). *Klinische Wochenschrift*, 1957, *35:* 19, pp. 974-980

G

GORDONOFF, T. : Analgesie und vegetatives Nervensystem (Analgesia and the vegetative nervous system. Analgésie et système nerveux végétatif). *Acta Neurovegetativa*, 1957, *16:* 1-4, pp. 384-389

GURFINKEL, M.; ALVARES, L. M. : Enfarte do miocárdio, anticoagulantes e analgesia potencializada (Myocardial infarct, anticoagulants and potentialized analgesia. Infarct myocardiaque, anticoagulants et analgésie potentialisée). *Medicina, Cirurgia, Farmacia*, 1958, No. 266, pp. 252-263

H

HOUGS, W.; SKOUBY, A. P. : The analgetic action of analgetics, antihistaminics and chlorpromazine on volunteers. *Acta Pharmacologica et Toxicologica*, 1957, *13:* 4, pp. 405-409

K

KEMPER, W. W. : Sôbre a prescricão de analgésicos contra as dôres de cabeça (Prescription of analgesics for headache. Prescription d'analgésiques contre les maux de tête). *Revista Brasileira de Medicina*, 1958, *15:* 1, pp. 58-60

KLEINSCHMIDT, G.; MOTHES, K. : Zur Züchtung eines Arzneimohns (Papaver Somniferum); vorläufige Mitteilung (Improvement of medical poppy (Papaver somniferum); preliminary report. De l'amélioration d'un pavot médicinal (Papaver somniferum); communication préliminaire). *Pharmazie*, 1958, *13:* 6, pp. 357-360

KURIAKI, K.; IWASE, K. : Ueber den Wirkungsmechanismus der Narkotika. II. Einflüsse der Narkotika und der zentralerregenden Mittel auf die Kalium- und Natriumverteilung und die Aktivität der Carbonhydrase im Hirn (Mechanism of action of narcotics. II. Effect of narcotics and central nervous system stimulants on potassium and sodium distribution and anhydrase activity in the brain. Mécanisme d'action des narcotiques. II. Effet des narcotiques et des stimulants du système nerveux central sur la distribution du potassium et du sodium et sur l'activité de l'anhydrase carbonique dans le cerveau). *Japanese Journal of Pharmacology*, 1957, *7:* 1, pp. 31-34

KURIAKI, K.; NAITO, T. : Die Verteilung der Histidindecarboxylaze in verschiedenen Gebieten des Zentralnervensystems und Effekte einiger Narkotika und Analeptica auf die Enzymaktivität (Distribution of histidine decarboxylase in various regions of the central nervous system and effects of some narcotics and analeptics on enzyme activity. Distribution de la décarboxylase de l'histidine dans diverses régions du système nerveux central et effets de certains analgésiques et analeptiques sur l'activité enzymatique). *N.-S. Archiv für experimentelle Pathologie und Pharmakologie*, 1958, *232:* 3, pp. 481-486

L

LA BARRE, J.; DESMAREZ, J. J. : Propriétés toxicomanogènes des dérivés des propylamines. *Archives internationales de Pharmacodynamie et de Thérapie*, 1958, *114:* 3-4, pp. 480-481

LANDE, A. : La codification du droit international des stupéfiants. *Annuaire français de droit international*, 1956, *2*, pp. 557-571

LINDESMITH, A. R. : Our immoral drug laws. *Nation*, 1958, *186*, pp. 558-562

LINDLEY, J. E.; ROGERS, S. F.; MOYER, J. H. : Analgesic-potentiating effect of chlorpromazine during labor. A study of 2093 patients. *Obstetrics and Gynecology*, 1957, *10:* 5, pp. 582-586

LIUBLINA, E. I. : Znachenie malykh doz bromistogo natrila pri deistvii porogovykh kontsentratsii narkotikov na vyshuiu nervnuiu delatel'nost krolika (Significance of small doses of sodium bromide following action of liminal doses of narcotics on the higher nervous activity. Signification de faibles doses de bromure de sodium suivant l'action de doses liminales de stupéfiants sur l'activité nerveuse supérieure). *Zhurnal vysshei nervnoi deiatel'nosti imeni I. P. Pavlova*, 1957, *7:* 3, pp. 447-450

M

McKENZIE, J. S. : Some pharmacological properties of pyrrolizidine alkaloids and their relationship to chemical structure. *Australian Journal of experimental Biology and medical Science*, 1958, *36:* 1, pp. 11-21

MARCUS, P. S.; WHITE, Jr, C. W.; MEGIRIAN, R. : A research evaluation of the ratio of narcotic to narcotic antagonist. *Current researches in Anesthesia and Analgesia*, 1958, *37:* 2, pp. 51-57

MASSICOT, J. : Sur une nouvelle méthode de détection des alcaloïdes du pavot par chromatographie sur papier. *Comptes rendus ... Académie des sciences*, 1958, *246:* 10, pp. 1622-1624

MATHIEU, E. : L'anesthésie générale dans la thyroïdectomie. *Anesthésie, Analgésie, Réanimation*, 1957, *14:* 3, pp. 511-517

MELLETT, E. B. : Cellular distribution of narcotic drugs. *Dissertation Abstracts*, 1958, *18:* 4, pp. 1456-1457

MODELL, W. : The search for a morphine substitute. *American Journal of Nursing*, 1957, *57:* 12, pp. 1565-1567

MOSKWA, W.; GRZYWACZ, M.: Oddziaływanie zwierząt naświetlonych promieniami Roentgena na niektóre nerkotyki (Reaction of animals irradiated with roentgen rays to certain narcotics. Réactions à certains narcotiques d'animaux irradiés aux Rayons X). *Acta physiologica polonica*, 1957, *8:* 3-3a, pp. 470-471

N

NIMB, M. : The consumption of narcotic drugs in Denmark, *Bulletin on Narcotics*, 1958, *10:* 3, pp. 1-5. La consommation des stupéfiants au Danemark. *Bulletin des stupéfiants*, 1958, *10:* 3, pp. 1-5

P

PAKYNTEIN, E. H. : Opium prohibition campaign in Assam. *Bulletin on Narcotics*, 1958, *10:* 3, pp. 12-14. La campagne pour la prohibition de l'opium en Assam. *Bulletin des stupéfiants*, 1958, *10:* 3, pp. 13-15

PEDRAZZOLI, A.; ROGGERO, M. : Antiartritici ed antiallergici (Antiarthritics and antiallergics. Antiarthritiques et antiallergiques). *Bollettino Chimico Farmaceutico*, 1958, *97:* 3, pp. 154-155

PELLIGRINI, R. : Lesioni farmacologiche del sistema nervoso centrale e attività transaminasica serica (Pharmacological lesions of the central nervous system and serum transaminase activity. Lésions pharmacologiques du système nerveux central et activité transaminasique sérique). *Sperimentale*, 1957, *107:* 4, pp. 260-270

PROOSDIJ-HARTZEMA, E. G. van; JONGH, D. K. de : A series of potent analgesics. *Acta Physiologica et Pharmacologica Neerlandica*, 1957, *5:* 4, pp. 398-405

R

REICHELT, J.; SARSUNOVA, M. : Identitätsnachweis einiger galenischen Präparate des Tschechoslovakischen Arzneibuches 2 (Identification of several galenical preparations from the Czechoslovakian Pharmakopoeia 2. Iden-

tification de quelques préparations galéniques de la Pharmacopée (2) tchéco-slovaque). *Pharmaceutisch Weekblad*, 1958, *93:* 4, pp.159-164

RICHARD, A. : Drogues et poisons, bases physiologiques de leurs utilisations. *Revue de pathologie générale et comparée*, 1955, No. 666, p. 361; No. 667, pp. 527-556

ROBEY, M. : L'hydroxyprégnanedione dans l'analgésie obstétricale. *Les entretiens de Bichat 1957. Chirurgie*, Paris, pp. 253-256

ROYERE, M. : Les drogues. *Libre pharmacie*, 1955, No. 102, pp. 10-13

S

SABA, G. M.; OPPO, G. T. : Esperienze cliniche con una nuova associazione analgesica nella cura del dolore post-operatorio in chirurgia ginecologica (Clinical tests of a new analgesic combination in therapy of postoperative pain in gynecological surgery. Expérimentation clinique d'une nouvelle combinaison analgésique pour le traitement de la douleur post-opératoire en chirurgie gynécologique). *Minerva ginecologica*, 1958, *10:* 8, pp. 309-317

SANGAILO, A. K.; DEN'GINA, N. D.; GORBASHEVA, M. P. : K vaprosu o kombinirovannom deistvii analgetikov s aminazinom (Combined effect of analgesics with aminazine. Effet combiné d'analgésiques avec l'aminazine). *Farmakologiia i Toksikologiia*, 1958, *21:* 3, pp. 10-12

SAUTER, A. : Der Analgeticamissbrauch als Problem des öffentlichen Gesundheitswesens (Misuse of analgesics as a problem of public health. L'abus des analgésiques considéré comme problème de santé publique). *Bulletin der Schweizerischen Akademie der medizinischen Wissenschaften*, 1958, *14:* 2, pp. 93-99

SCHAUMANN, W. : Zusammenhänge zwischen der Wirkung der Analgetika und Sympathicomimetica auf den Meerschweinchen-Dünndarm (Relationship between the effects of analgesics and sympathomimetics on guinea pig small intestines. Rapport entre les effets des analgésiques et des sympathomimétiques sur le petit intestin du cobaye). *N.-S. Archiv für experimentelle Pathologie und Pharmakologie*, 1958, *233:* 1, pp. 112-124

SCHICK, E.-R.; REIMANN-PHILIPP, R. : Die Züchtung von Heilpflanzen (Sammelreferat) (Improvement of medicinal plants (Survey). L'amélioration des plantes médicinales (Revue)). *Züchter*, 1957, *27:* 7, pp. 300-332

SCHORER, F. : Altersveränderungen und ihre Berücksichtigung bei der Anaesthesie (Effects of age and their influence during anaesthesia. Effets de l'âge et leur influence au cours de l'anesthésie). *Anaesthesist*, 1957, *6:* 6, pp. 381-386

SCHULZ, R. : Ueber die Behandlung der Opiatvergiftung mit Nalorphine beim Kind (Therapy of opiate poisoning by nalorphine in a child. Traitement avec de la nalorphine de l'intoxication opiacée chez l'enfant). *Archiv für Kinderheilkunde*, 1958, *157:* 1, pp. 60-64

T

* TAKAGI, K.; KAMEYAMA, T. : (Study of analgesics. II Determination of analgesic activity by the heating plate method. Etudes sur les analgésiques. II. Détermination de l'activité analgésique par la méthode de la plaque chauffante). *Journal of the Pharmaceutical Society of Japan*, 1957, *77:* 8, pp. 871-875

THIES, H.; SORGENFREY, C. H. : Ueber die spectrophotometrische Bestimmung von Alkaloiden im ultravioletten Spektralbereich bei 2537 Å (Spectrophotometric determination of alkaloids in ultraviolet spectrum range at 2537 angstroms. Détermination spectrophotométrique des alcaloïdes dans la région du spectre à 2537 angstroms ultraviolets). *Archiv der Pharmazie und Berichte der Deutschen pharmazeutischen Gesellschaft*, 1958, *291:* 63 (2), pp. 68-76

V

VAILLE, C. : Les stupéfiants, problème international. *Semaine médicale professionnelle et médico-sociale*, 1957, *33:* 32-33 pp. 1221-1238; *34*, pp. 1265-1278; 35, pp. 1301-1313

VALETTE, G.; ETCHEVERRY, J. : Etude comparée de l'effet de différents analgésiques par voie percutanée chez la Souris. *Annales pharmaceutiques françaises*, 1957, *15:* 12, pp. 683-691

VANDAM, L. D.; McLEMORE Jr., G. A. : Circulatory arrest in patients with complete heart block during anesthesia and surgery. *Annals of internal medicine*, 1957, *47:* 3, pp. 518-532

W

WANG, R. I.; GRUBER Jr., C. M. : A double-blind method for evaluating analgesics in man. *American Journal of the medical sciences*, 1958, *235:* 3, pp. 297-300

WEIDEMANN, H. E. : Die Verschreibung von Betäubungsmitteln : Zustand und Probleme; dargestellt an Hand von Untersuchungen in einem Kreis über einen Zeitraum von drei Jahren (Prescription of narcotics, state and problems, as observed in a county during a three-year period. Prescription des stupéfiants; position et problèmes d'après les recherches faites dans un canton pendant une période de trois ans). *Deutsche Gesundheitswesen*, 1958, *13:* 3, pp. 78-87

WHO : Expert Committee on Addiction-producing drugs; eighth report. *Technical Reports Series*, 1958, *142:* pp. 1-2

WILSON, E. : Simplified control of narcotics. *Canadian Hospital*, 1958, *35:* 5, pp. 51-52; passim

WRIGHT, A. E. : The battle against opium in Iran. *Bulletin on Narcotics*, 1958, *10:* 2, pp. 8-11. La lutte contre l'usage de l'opium en Iran. *Bulletin des Stupéfiants*, 1958, *10:* 2, pp. 8-11

Z

ZIPF, H. F.; REICHERTZ, P. : Zur Auswertung von Endoanaesthetica durch Wirkung/Zeit-Kurven (Evaluation of general anaesthetics by means of action/time curves. Evaluation de l'activité des anesthésiques généraux au moyen des courbes action/temps. *N.-S. Archiv für experimentelle Pathologie und Pharmakologie*, 1957, *232:* 1, pp. 304-305

ZYKA, J. : Polarometric (amperometric) titration in the analysis of narcotic substances. *Bulletin on Narcotics*, 1958, *10:* 1, pp. 35-38. Le titrage polarimétrique (ampérométrique) dans l'analyse des stupéfiants. *Bulletin des stupéfiants*, 1958, *10:* 1, pp. 38-42

Part II. — OPIUM POPPY, OPIUM AND DRUGS MANUFACTURED THEREFROM
PAVOT A OPIUM, OPIUM ET DROGUES QUI EN SONT TIRÉES

A. Opium poppy, opium and opium alkaloids collectively considered — Pavot à opium, opium et alcaloïdes de l'opium considérés dans leur ensemble

A

ABDEL-RAHMAN, A. A. : Anwendung der Papierchromatographie auf einige Opiumalkaloide und einige Morphinderivate (Application of paper chromatography to some opium alkaloids and morphine derivatives. Application de la chromatographie sur papier à quelques alcaloïdes de l'opium et dérivés de la morphine). *Archiv der Pharmazie und Berichte der Deutschen Pharmazeutischen Gesellschaft*, 1957, *290*/62 : 7, pp. 321-325

ABDEL-RAHMAN, A. A. : Trennung der Inhaltsstoffe der Opiumtinktur, Pantopon- und Spasmalginampullen durch Papier-chromatographie (Separation of the ingredients of opium tincture, pantopon and spasmalgin ampullae by paper chromatography. Séparation des ingrédients de la teinture d'opium, du pantopon et d'ampoules de spasmalgine par la chromatographie sur papier). *Archiv der Pharmazie und Berichte der Deutschen Pharmazeutischen Gesellschaft*, 1957, *290*/62 : 7, pp. 326-329

ANONYMOUS — ANONYME : Noscapine. *Journal of the American Medical Association*, 1958, *167:* 8, pp. 993-994

AUROUSSEAU, M.; NAVARRO, J. : Etude comparative de la toxicité aiguë de quelques alcaloïdes dérivés de l'opium. *Annales pharmaceutiques françaises*, 1957, *15:* 11, pp. 640-653

AWE, W.; WINKIER, W. : Ueber die Alkaloide des Klatschmohns (Alkaloids of Corn Poppy. Alcaloïdes du coquelicot). *Archiv der*

Pharmazie und Berichte der Deutschen pharmazeutischen Gesellschaft, 1957, *290*/62 : 8-9, pp. 367-376

B

BATTERSBY, A. R.; HARPER, B. J. T.: Origin of the methyl groups in morphine, codeine and thebaine. *Chemistry and Industry*, 1958, *2*, p. 365

BHATTACHARJEE, B.; AGARWAL, R. K. : N-allyl-normorphine in opium poisoning. *Journal of the Indian Medical Association*, 1957, *29:* 9, pp. 367-368

BOISSIER, J. R. : Quand et comment prescrire les opiacés? *Vie médicale*, 1958, *39*, p. 31; passim

BROCHMANN-HANSSEN, E. : Aktuelle problemer i forbindelse med opiumsvalmnen (Present problems in connection with the opium poppy. Problèmes actuels concernant le Pavot à opium). *Meddelelser fra norsk farmaceutisk Selskap*, 1957, *19:* 7, pp. 113-128

BURCHARD, J. M. : Pharmakopsychiatrische Untersuchungen über die Wirkungsweise der Opiumalkaloide bei endogenen Psychosen (Pharmacopsychiatric studies on the mechanism of action of opium alkaloids in endogenous psychoses. Etudes pharmaco-psychiatriques sur le mécanisme d'action des alcaloïdes de l'opium sur les psychoses endogènes). *Nervenarzt*, 1958, *29:* 3, pp. 103-110

D

DÖNHARDT, A. : Die Behandlung der Schlafmittel- und Alkaloid- Vergiftungen (Therapy of poisoning caused by hypnotics and alkaloids. Traitement des empoisonnements dus aux hypnotiques et aux alcaloïdes). *Therapie der Gegenwart*, 1957, *96:* 7, pp. 249-251

E

ELTUTAR, H. & IGNECILER, M. : Researches on various kinds of fungi observed on Turkish opium, their action on the quality of opium and their removal with different sorts of fungicides. *Bulletin on Narcotics*, 1958, *10:* 4, pp. 12-16. Recherches sur les variétés de champignons observées sur l'opium turc et leur action sur la qualité du produit et leur élimination à l'aide de divers produits fongicides. *Bulletin des stupéfiants*, 1958, *10:* 4, pp. 13-17

F

FEJKLOVÁ, M.; BARKOVÁ, K. : Anatomische Studien über die Milchröhren bei Papaver somniferum L. während der Vegetationszeit (Anatomical study of the lactiferous ducts in Papaver somniferum L. during vegetation. Etude anatomique des conduits lactifères de Papaver somniferum L. durant le cycle végétatif). *Pharmazie*, 1958, *13:* 4, pp. 220-229

FISCHER, R.; OTTERBECK, N. : Zum Nachweis von Analgeticis (Opium-Alkaloiden, deren Derivaten und synthetischen Substanzen) mittels " Test-Tube " - Chromatographie (Test-tube chromatography in determination of analgesics (Opium alkaloids, derivatives and synthetic substances). Mise en évidence d'analgésiques (alcaloïdes de l'opium, leurs dérivés et substances synthétiques) au moyen de la microchromatographie (tube-test)). *Scientia pharmaceutica*, 1957, *25:* 4, pp. 242-248

G

GINSBURG, D. : Some recent advances in the chemistry of the opium alkaloids. *Bulletin on Narcotics*, 1958, *10:* 2, pp. 1-5; Progrès récents de la chimie des alcaloïdes de l'opium. *Bulletin des stupéfiants*, 1958, *10:* 2, pp. 1-5

H

HAKIM, S. A. E. : Extraction and detection of poppy alkaloids. *Journal of Physiology*, 1957, *138:* 2, p. 8. Poppy alkaloids and glaucoma. *Ibid.*, p. 40 P-41 P

HEEGER, E. F. : Zur Problematik des Anbaus von *Papaver somniferum* L. (Mohn) als Rohstoff für die pharmazeutisch-chemische Industrie (Problems of the culture of *Papaver somniferum* L. (Poppy) as raw material for the pharmaceutico-chemical industry. Problèmes de la culture du *Papaver somniferum* L. (pavot) comme matière première pour l'industrie pharmaceutico-chimique). *Die Pharmazie*, 1957, *12:* 5, pp. 287-290

K

KELENTEY, B.; STENSZKY, E.; CZOLLNER, F.; SZLÁVIK, L.; MÉSZÁROS, Z. : Darstellung und pharmakologische Untersuchungen der N-Oxyde der Opium-Alkaloide (Preparation and pharmacological investigation of N-oxides of opium alkaloids. Préparation et études pharmacologiques des N-oxydes des alcaloïdes de l'opium). *Arzneimittel-Forschung*, 1957, *7:* 10, pp. 594-597

KELENTEY, B.; STENSZKY, E.; CZOLLNER, F.; SZLÁVIK, L.; MÉSZÁROS, Z. : Opiumalkaloidak N-oxidjainak elöállitása és pharmacológiai tulajdonságai (Preparation and pharmacological properties of N-oxides of opium alkaloids. Préparation et propriétés pharmacologiques des N-oxides des alcaloïdes de l'opium). *Kísérletes orvostudomány*, 1958, *10:* 1, pp. 70-77

KOPP, E. : Versuche zur Züchtung einer morphinreichen Mohnsorte (Attempts to cultivate a poppy strain rich in morphine. Essais en vue de produire une variété de pavot riche en morphine). *Pharmazie*, 1957, *12:* 9, pp. 614-620

L

* LISOVSKIJ, G. M. : (Structure anomalies in perianth of *Papaver somniferum*. Anomalies de la structure du périanthe chez Papaver somniferum L.). *Botanicheskii Zhurnal*, 1957, *42:* 8, pp. 1282-1285

M

MAHESHWARI, NIRMALA : In vitro culture of excised ovules of Papaver somniferum. *Science*, 1958, *127:* 3294, p. 342

MARANGONI, P. : Sull'esame microscopico e chimico della polvere di oppio (Microscopical and chemical assay of opium powder. Examen microscopique et chimique de la poudre d'opium). *Annali di Chimica farmaceutica*, 1938, 7, pp. 77-87

MASSICOT, J. : Sur une nouvelle méthode de détection des alcaloïdes du Pavot par chromatographie sur papier. *Comptes rendus ... Académie des sciences*, 1958, *246:* 10, pp. 1622-1624

N

NIKONOV, G. K. : Accumulation and distribution of the main alkaloids in the opium poppy in the course of its ontogenesis. *Bulletin on Narcotics*, 1958, *10:* 1, pp. 20-24. Accumulation et distribution des alcaloïdes principaux dans le pavot à opium au cours de son ontogénèse. *Bulletin des stupéfiants*, 1958, *10:* 1, pp. 22-26

P

PFEIFER, S. : The quantitative assay of the principal alkaloids in the poppy and in opium. *Bulletin on Narcotics*, 1958, *10:* 3, pp. 18-33. La détermination micro-quantitative des principaux alcaloïdes du pavot et de l'opium. *Bulletin des stupéfiants*, 1958, *10:* 3, pp. 19-35

PFEIFER, S. : Ueber die quantitative Erfassung der wichtigsten Mohnalkaloide im Mikromasstab (Quantitative determination of small amounts of important opium alkaloids. Détermination quantitative de quantités infimes des alcaloïdes les plus importants de l'opium). *Pharmazie*, 1958, *13:* 2, pp. 100-109

* POPOV, M. G. : (Study of relationship between *Papaver* and *Roemeria* genera and their history. Contribution aux rapports mutuels entre les genres Papaver et Roemeria et à leur histoire). *Botanicheskii Zhurnal SSSR*, 1957, *42:* 9, pp. 1389-1397

S

SÁRKANY, S.; DANOS, B. : Ueber die Veränderungen im Morphin- und Nebenalkaloiden-Gehalt in den verschiedenen Organen der Mohnpflanze während der Vegetationsperiode. I (Variations in the morphine and other alkaloid content of various organs of Poppy plant during its growth. Sur les variations de la teneur en morphine et en alcaloïdes accessoires dans les différents organes du Pavot au cours de la période de végétation. I). *Acta Botanica Academiae Scientiarum Hungaricae*, 1957, *3:* 3-4, pp. 293-316

* SHAVROV, L. A. : (Anomalies in structure of reproductive organs in flower of some Papaver species. Anomalies dans la structure des organes reproducteurs de la fleur du Pavot Papaver spp.). *Botanicheskii Zhurnal*, 1957, *42:* 8, pp. 1249-1253

SHEVELEV, V. A.; BANKOVSKY, A. I. & MURAVYOVA, V. I. : Mechanical drying of raw opium. *Bulletin on Narcotics*, 1958, *10:* 2, pp. 6-7; Séchage mécanique de l'opium brut. *Bulletin des stupéfiants*, 1958, *10:* 2, pp. 6-7

SICHENEDER, T. : Beitrag zur Behandlung überwiegend psychogen-bedingter Abdominalsymptome (Treatment of abdominal symptons of predominantly psychogenic origin. Traitement de symptômes abdominaux d'origine psychogénique prédominante). *Medizinische*, 1958, No. 3, pp. 133-134

STENZEL, E. : Zur Sicherung der Mohnalkaloidproduktion (To ensure the (sufficient) production of poppy alkaloids. Pour nous assurer d'une production (suffisante) d'alcaloïdes du pavot). *Die Pharmazie*, 1957, *12:* 5, pp. 286-287

B. Morphine

A

ADELMAN, M. H. & ROSENTHAL, A. I. : Nalorphine in the treatment of morphine-induced biliary colic. *Journal of the Mount Sinai Hospital*, 1958, *25:* 1, pp. 36-37

ADLER, T. K.; ELLIOTT, H. W. & GEORGE, R. : Some factors affecting the biological disposition of small doses of morphine in rats. *Journal of Pharmacology and Experimental Therapeutics*, 1957, *120:* 4, pp. 475-487

ANGELUCCI, L. : Influence of cocarboxylase on tolerance to morphine in the rat. *Nature*, 1958, *181:* 4614, pp. 967-968

ARKO, H.; KIVALO, E. & RINNE, U. K. : Neuro- secretory substance in the neurohypophysis of the rat; influence of some antidiuretic drugs. *Annales medicinae experimentalis et Biologiae Fenniae*, 1957, *35:* 4, pp. 404-408

B

BACQ, Z. M. & FISCHER, P. : The action of various drugs on the suprarenal response of the cat to total-body X-irradiation. *Radiation Research*, 1957, *7:* 4, pp. 357-364

BAKER, W. P. & WOODS, L. A. : A study in the dog of the renal clearance of morphine and the effect of morphine on p-aminohippurate clearance. *Journal of Pharmacology and experimental Therapeutics*, 1957, *120:* 3, pp. 371-374

BATTERSBY, A. R. & HARPER, B. J. T. : Biogenesis of morphine. *Chemistry and Industry*, 1958, No. 2, pp. 364

BEACH, H. D. : Some effects of morphine on habit function. *Canadian Journal of Psychology*, 1957, *11:* 3, pp. 193-198

BEACH, H. D. : Effect of morphine on the exploratory drive. *Canadian Journal of Psychology*, 1957, *11:* 4, pp. 237-244

BERTELLI, A.; BUTTI, G. & GORI, E. : Attività della 2-etil-cis-crotonilurea su alcuni tipi di neuroeccitazione centrale (Action of 2-ethyl-cis-crotonylurea on various types of central nervous stimulation. Activité de l'éthyl-2-cis-crotonyl urée sur quelques types d'excitation nerveuse centrale). *Bollettino della Società italiana di Biologia sperimentale*, 1957, *33:* 6, pp. 892-895

BOSE, B. C.; GUPTA, S. S.; VIJAYVARGIYA, R. & JALNEWALLA, K. M. : Observations on the pharmacological activity of different salts of adrenaline, morphine and strychnine. *Indian Journal of medical Research*, 1958, *46:* 2, pp. 193-198

C

CHOWDHURI, B. N. & SEN, S. P. : Inhibitory effect of hydrocortisone and morphine on corticotrophin secretion in normal stressed rats. *Journal of the Indian Medical Association*, 1957, *29:* 7, pp. 274-277

CHRISTIE, G.; GERSHON, S.; GRAY, R.; SHAW, F. H.; McCANCE, I. & BRUCE, D. W. : Treatment of certain side-effects of morphine. *British medical Journal*, 1958, No. 5072, pp. 675-680

D

DESSI, P. & GIANNI, A. M. : Sulle interazioni della morfina e della mescalina con le proteine cerebrali (Interactions of morphine and mescaline with cerebral proteins. Interactions de la morphine et de la mescaline avec les protéines du cerveau). *Archivio Italiano di Scienze Farmacologiche*, 1957, *7:* 2, pp. 93-97

DI CARLO, F. : Progressi nel trattemento del barbiturismo (Progress in the treatment of barbiturate poisoning. Progrès dans le traitement de l'intoxication barbiturique). *Riforma medica*, 1958, *72:* 8, pp. 211-214

DMOCHOWSKI, J.: Wpływ morfiny i dolantyny na czynność oddechową w zależności od dużych dawek largaktylu (Effect of large doses of largactil on respiratory reactions to morphine and dolantin. Action du largactil en hautes doses sur les réactions respiratoires à la morphine et la dolantine). *Acta Physiologica pólonica*, 1957, *8:* 3-3a, pp. 311-312

DORDONI, F. : Aspetti teorici e pratici dei moderni antagonisti della morfina (Theoretical and practical aspects of modern antagonists of morphine. Aspects théoriques et pratiques de l'étude des antagonistes modernes de la morphine). *Archivio italiano di Scienze Farmacologiche*, 1958, *8:* 1, pp. 3-34

DRIPPS, R. D.; MILLAR, R. A. & KNEALE, D. H. : A comparison of anileridine, morphine, and meperidine in man. *Surgery, Gynecology and Obstetrics*, 1957, *105:* 3, pp. 322-326

DUCKWORTH, M. W. & RYMAN, B. E. : Metabolic changes in tissues of the rat in acute and chronic morphinisation. *Archives internationales de Pharmacodynamie et de Thérapie*, 1957, *113:* 1-2, pp. 127-135

E

ECKENHOFF, J. E. & NORTON, M. L. : The treatment of intractable pain with large doses of morphine and amiphenazole (daptazole). *Acta Anaesthesiologica Scandinavica*, 1958, *2:* 1, pp. 45-51

F

FEJFAR, Z.; BERGMANN, K.; FEJFAROVA, M. & VALACH, A. : The effect of morphine on pulmonary haemodynamics in mitral stenosis. *Cardiologia*, 1957, *31:* 5, pp. 461-468

FERRARIO, L. & PALMIERI, R. : Sulla possibilitá di combattere la depressione respiratoria da analgesici durante l'anestesia generale mediante l'impiego di alcuni farmaci (Possibility of combating respiratory depression from analgesics during general anaesthesia by the use of certain drugs. Possibilité de combattre au moyen de certaines drogues la dépression respiratoire due aux analgésiques durant l'anesthésie générale). *Minerva anestesiologica*, 1958, *24:* 2, pp. 57-64

FROMMEL, E. : Du rôle du diencéphale et des centres du vague au cours des stress traumatiques, de la brûlure, de l'hypothermie et de l'hyperthermie (morphine, chlorpromazine, ACTH et cholinergie). *Presse médicale*, 1957, *65:* 71, pp. 1585-1586

FUJIMOTO, J. M. & WAY, E. L. : Isolation and crystallization of " bound " morphine from urine of human addicts. *Journal of pharmacology and experimental Therapeutics*, 1957, *121:* 3, pp. 340-346

FUJIMOTO, J. M. & WAY, E. L. : Studies on the structure of " bound " morphine. *Journal of the American Pharmaceutical Association, sc. ed.*, 1958, *47:* 4, pp. 273-275

G

GANGLOFF, H. & MONNIER, M. : The topical action of morphine, levorphanol (levorphan) and the morphine antagonist levallorphan on the unanesthetized rabbit's brain. *Journal of Pharmacology and experimental Therapeutics*, 1957, *121:* 1, pp. 78-95

GARRATT, D. C.; JOHNSON, C. A. & LLOYD, C. J. : The determination of morphine in opium and some of its galenical preparations. *Journal of Pharmacy and Pharmacology*, 1957, *9:* 12, pp. 914-928

GERSHON, S. & SHAW, F. H. : Morphine and histamine release. *Journal of Pharmacy and Pharmacology*, 1958, *10:* 1, pp. 22-29

GERSHON, S.; BRUCE, D. W.; ORCHARD N. & SHAW, F. H. : Amiphenazole and morphine in production of analgesia. *British Medical Journal*, 1958, No. 5092, pp. 366-368

GRIESSER, G. : Ueber die Hemmung der Antidiuretischen Wirkung von Morphin und Dromoran durch (—)-3-Hydroxy-N-allyl-Morphinan (Laevallorphan) beim Menschen (Inhibition in man of antidiuretic action of morphine and of Dromoran by means of (—) 3-hydroxy-N-allylmorphinane. Sur l'inhibition, chez l'Homme, de l'action antidiurétique de la morphine et du Dromoran par le (—) hydroxy-3-N-allyl-morphinane (Lévallorphan). *Klinische Wochenschrift*, 1957, *35:* 17, pp. 851-855

GRUHZIT, C. C. : Chemoreflex activity of dextromethorphan (romilar), dextrorphan, codeine and morphine in the cat and the dog. *Journal of Pharmacology and Experimental Therapeutics*, 1957, *120:* 4, pp. 399-407

H

HÄUSSERMANN, H. & SCHECKER, H. J. : Hat Sertürner reines Morphin isoliert? Zur papierchromatographischen Reinheitsprüfung von Alkaloïden (Has Serturner isolated pure morphine? Paper chromatographic purity tests for alkaloids. Serturner a-t-il isolé la morphine pure? Test de pureté des alcaloïdes par la chromatographie sur papier). *Archiv der Pharmazie und Berichte der Deutschen Pharmazeutischen Gesellschaft*, 1957, *290: 62* (10), pp. 509-516

HILL, H. E.; PESCOR, F. T.; BELLEVILLE, R. E. & WIKLER, A. : Use of differential bar-pressing rates of rats for screening analgesic drugs. I. Techniques and effects of morphine. *Journal of Pharmacology and Experimental Therapeutics*, 1957, *120:* 3, pp. 388-397

HOCHULI, E. : Lorfan als Morphinantagonist in Gynäkologie und Geburtshilfe (Lorfan as a

morphine antagonist in gynecology and obstetrics. Le Lorfan comme antagoniste de la morphine en gynécologie et en obstétrique). *Schweizerische medizinische Wochenschrift*, 1957, *87:* 43, pp. 1327-1332

HÖRTNAGL, W. : Ueber ein neues spezifisches Antidot bei der schweren Morphiumvergiftung (New specific antidote in severe morphine poisoning. Un nouvel antidote spécifique de l'empoisonnement morphinique grave). *Wiener klinische Wochenschrift*, 1957, *69:* 28, pp. 506-507

HOSOYA, E. & BRODY, T. M. : *In vitro* oxidation of morphine by rat tissue homogenates. *Journal of Pharmacology and Experimental Therapeutics*, 1957, *120:* 4, pp. 504-511

* HSU BIN, KIN KUO-CHANG : (Study of pharmacological actions of Corydalis. II. Tolerance to Corydalis B and L. Etude sur les actions pharmacologiques de Corydalis. II. Tolérance aux corydalis B et L.) *Acta physiologica sinica*, 1957, *21:* 2, pp. 158-162

HUGGINS, R. A.; SPENCER, W. A.; GEDDES, L. A.; DEAVERS, S & MOYER, J. H. : Respiratory functions in man following intravenous administration of morphine, N-allylnormorphine, and N-allylnormorphine after morphine. *Archives internationales de Pharmacodynamie et de Thérapie*, 1957, *111:* 3, pp. 275-292

HUPERZ, R. : Erfahrungen mit einem neuartigen Hustenmittel in der Kinderpraxis (Experience with a new cough mixture in pediatric practice. Expériences avec un nouvel anti-tussif en pédiatrie). *Medizinische*, 1958, No. 27-28, pp. 1105-1106

I

IVANENKO, E. F. : Vliianie narkoza na izmeniia temperatury kory bol'shikh polusharii golovnogo mozga (Influence of general anaesthesia on intracerebral temperature changes. Influence de l'anesthésie générale sur les variations de la température intracérébrale). *Fiziologicheskii Zhurnal SSSR*, 1957, *43:* 9, pp. 851-857

J

JANSSEN, P. A. J. & JAGENEAU, A. H. : A new series of potent analgesics : dextro 2 : 2-diphenyl-3-methyl-4-morpholinobutyryl-pyrrolidine and related basic amides. II. Comparative analgesic activity, acute toxicity and tolerance development in rats for R 875, morphine, pethidine and methadone. *Journal of Pharmacy and Pharmacology*, 1958, *10:* 1, pp. 14-21

K

KASE, Y.; YUIZONO, T.; SERIKAWA, H.; YAMAMOTO, S.; YAMASAKI, T.; FUSHIMIZU, T.; KATAYAMA, N.; MORIYA, T. & NOZUHARA, T. : d-3-dimethylamino-1, 1-diphenylbutyl ethyl sulfone as a long-acting antitussive. *Chemical and Pharmaceutical Bulletin of Japan*, 1958, *6:* 1, pp. 109-111

KLEINSCHMIDT, G. : Nachweis des Morphins in Papaver Setigerum DC (Demonstration of morphine in Papaver setigerum DC. Identification de morphine dans le Papaver setigerum DC). *Archiv der Pharmazie und Berichte der Deutschen pharmazeutischen Gesellschaft*, 1958, *291:* 63 (2), pp. 109-111

KOPF, F. & MØLLER NIELSEN, I. : Pharmacology and toxicology of captodiamine (p-butyl-mercaptobenzhydryl-β-dimethylamino-ethylsulphide) *Arzneimittel-Forschung*, 1958, *8:* 3, pp. 154-159

KOSTERLITZ, H. W.; ROBINSON, J. A. & TAYLOR, D. W. : Inhibition of autonomic neuro-effector transmission by morphine. *Journal of Physiology*, 1957, *139:* 2, pp. 28 P-29 P

KRUGLOV, N. A. : Antagonizm N-allilnormorfina i daftazola po otnesheniiu k morfinu (Antagonism of N-allylnormorphine and daphtazole to morphine. Antagonisme de l'N-allylnormorphine et du daphtazole à la morphine). *Farmakologiia i Toksikologiia*, 1958, *20:* 6, pp. 40-46

L

LA BARRE, J. : A propos des propriétés analeptiques circulatoires et respiratoires du diaminophénylthiazol au cours de l'intoxication morphinique du lapin. *Archives Internationales de Pharmacodynamie et de Thérapie*, 1957, *110:* 4, pp. 465-471

LECOMTE, J. : Influence des excitants et des dépresseurs centraux sur le choc anaphylactique du lapin. *Archives internationales de physiologie et de biochimie*, 1957, *65:* 3, pp. 451-458

LYNCH, T. A. & MEYERS, D. B. : A study of the selective antagonism by N-allylnormorphine against meperidine, methadone and morphine. *Journal of the American Pharmaceutical Association, Sc. Ed.*, 1958, *47:* 5, pp. 323-325

M

McGUIRE, T. A.; ETTEN, C. H. VAN; EARLE, F. R. & SENTI, F. R. : Use of ion exchange in recovery and partial purification of morphine from aqueous extracts of poppy capsules. *Journal of the American Pharmaceutical Association, Scientific Edition*, 1957, *46:* 4, pp. 247-248

MACRIS, S. G.; GRAVENSTEIN, J. S.; REICHLE, C. W. & BEECHER, H. K. : Drug synergism (potentiation) in pain relief in man : papaverine and morphine. *Science* (Wash.), 1958, *128:* 3315, pp. 84-85

MACRIS, S. G.; SMITH, G. M. & BEECHER, H. K. : Comparison of the antipruritic effect of morphine and papaverine in experimental and pathological itch in man. *Journal of Pharmacology and experimental Therapeutics*, 1958, *123:* 3, pp. 220-223

* MATSUMOTO, K. : (Morphine titration by the ion exchangers method. Analyse pharmaceutique polarographique. XVI. Dosage de la morphine à l'aide de méthode d'échanges d'ions). *Journal of the pharmaceutical Society of Japan*, 1957, *77:* 4, pp. 367-370

MAURATH, J. & RÜGER, R. : Kann die atemdepressive Wirkung des Morphiums durch Allyl-Derivate des Morphins verhindert werden? (Can the allyl derivates of morphine prevent its respiratory depressant action? L'action dépressive respiratoire de la morphine peut-elle être inhibée par les dérivés allyliques de la morphine?) *Arzneimittel-Forschung*, 1957, *7:* 11, pp. 665-672

MEDAKOVIĆ, M. : Antagonism of morphine towards 5-hydroxytryptamine. *Acta Medica Iugoslavica*, 1957, *11:* 1-2, pp. 186-189

MEHLTRETTER, C. L. & WEAKLEY, F. B. : Extraction of morphine from poppy capsules and its recovery by ion exchange. *Journal of the American Pharmaceutical Association, Scientific Edition*, 1957, *46:* 3, pp. 193-196

MERCIER, J. & SHAW, F. H. : Antagonisme entre la morphine et le 2,4-diamino-5-phénylthiazole (daptazole) au niveau du centre respiratoire et des systèmes qui contrôlent l'état vigile. *Thérapie*, 1957, *12:* 4, pp. 493-502

MURANO, T. & TANAKA, F. : Possible roles of the central nervous system in the action of morphine on blood pressure. *Japanese Journal of Pharmacology*, 1957, *6:* 2, pp. 94-104

N

NADEAU, G. & SOBOLEWSKI, G. : Une nouvelle méthode de dosage de très petites quantités de morphine. *Canadian Journal of Biochemistry and Physiology*, 1958, *36:* 6, pp. 625-631

NAITO, T. & KURIAKI, K. : Die Verteilung der Histidindecarboxylase in verschiedenen Gebieten des Zentralnervensystems und Effekte einiger Narkotica und Analeptica auf die Enzymaktivität (Distribution of histidine decarboxylase in various regions of the central nervous system and effects of some narcotics and analeptics on enzyme activity. La répartition de l'histidinedécarboxylase en divers points du système nerveux central et les effets de quelques narcotiques et analeptiques sur l'activité enzymatique). *Archiv für experimentelle Pathologie und Pharmakologie*, 1958, *232:* 3, pp. 481-486

O

O'RIORDAN, E. F. & BREWARD, A. D. : A comparison of barbiturate antagonists in thiopentone anaesthesia. *Anesthesia and Analgesia, Current researches*, 1958, *37:* 3, pp. 126-129

ORSINI, S. : Esametonio e spasmo morfinico (Hexamethonium and morphinic spasm. Hexaméthonium et spasme morphinique). *Medicina Sperimentale*, 1957, *31:* 4, pp. 411-416

P

PAERREGAARD, P. : A new method for quantitative determination of small amounts of morphine in human urine. *Acta Pharmacologica et Toxicologica*, 1957, *14* (1), pp. 38-52

PAERREGAARD, P. : Excretion of morphine in the urine of non-addicts. *Acta Pharmacologica et Toxicologica*, 1957, *14:* 1, pp. 53-57

PAPPER, S.; SAXON, L.; BURG, M. B.; SEIFER, H. W. & ROSENBAUM, J. D. : The effect of morphine sulfate upon the renal excretion of water and solute in man. *Journal of Laboratory and Clinical Medicine*, 1957, *50:* 5, pp. 692-704

PFEIFFER, J. : Die Pharmakoradiographie des Intestinaltraktes und ihre klinische Bedeutung speziell in der Magendiagnostik (Pharmacoradiography of the gastrointestinal tract and its clinical significance, with special reference to diagnosis of gastric disorders. Pharmacoradiographie du tube gastrointestinal et sa signification clinique, particulièrement en ce

qui concerne le diagnostique des troubles gastriques). *Münchener medizinische Wochenschrift*, 1957, *99:* 46, pp. 1701-1705

POLLI, J. F. & MUSIKER, S. : Effect of morphine, aerosol mixtures, and other agents on experimental pulmonary edema in rats following exposure to chlorine gas. *Experimental Medicine and Surgery*, 1958, *16:* 1, pp. 73-78

PORTOLANO, F.; CALIFANO, G. & DE FANIS, L. : Ricerche cliniche sul comportamento di alcuni indici della funzione surrenalica in rapporto alla preanestesia (Clinical research on the behaviour of various indices of adrenal function in relation to preanesthesia. Recherche clinique sur le comportement de divers indices de la fonction adrénale par rapport à la pré-anesthésie). *Rassegna Internazionale di Clinica e Terapia*, 1957, *37:* 20, pp. 936-941

PROOSDIJ-HARTZEMA, E. G., van : Le phénomène de Straub chez la souris; son analyse statistique et son application pratique pharmacologique. *Journal de Physiologie*, 1958, *50:* 2, pp. 464-469

PRUNER, G. : Determination of morphine in poppy capsules. *Bulletin on Narcotics*, 1958, *10:* 3, pp. 34-36; Détermination de la morphine dans les capsules du pavot. *Bulletin des stupéfiants*, 1958, *10:* 3, pp. 36-38

R

RAKHMAN, L. E. : Izmenenie ustoichivosti organisma k krovopotere pod vliianiem vnutrivennogo vvedeniie novokaina i morfina (Effect of intravenous administration of novocaine and morphine on resistance of the organism to blood loss. Effet de l'administration intraveineuse de novocaïne et de morphine sur la résistance de l'organisme aux pertes de sang). *Voenno-meditsinskii Zhurnal*, 1957, No. 11, pp. 28-31

REYNOLDS, A. K. & RANDALL, L. O. : *Morphine and allied drugs*. 1957, Toronto University Press (London : Oxford University Press) 393 pp. (xiii) ill.

ROBINSON, S. M. & JENKINS, H. J. : An investigation of the possible potentiation of the analgetic properties of morphine by mephenesin. *Journal of the American Pharmaceutical Association, Scientific Edition*, 1957, *46:* 9, pp. 556-558

ROUHIER, G. : Deux cas de gangrène gazeuse foudroyante à la suite d'injections medicamenteuses banales; leur pathogénie exogène ou endogène et l'importance médico-légale de cette pathogénie. *Bulletin de l'Académie nationale de Médecine*, 1958, *142:* 5-6, pp. 152-157

S

SADOVE, M. S. & SCHIFFRIN, M. J. : Clinical principles for the narcotic antagonists. *Postgraduate medicine*, 1957, *22:* 6, pp. 566-571

SÁMEL, M. : Blocking effect of morphine on the secretion of thyroid-stimulating hormone in rats. *Nature*, 1958, *181:* 4612, pp. 845-846

SAXENA, P. N. & GUPTA, G. P. : Potentiating effect of prostigmine on morphine-induced analgesia. *Indian Journal of Medical Research*, 1957, *45:* 3, pp. 319-325

SCARBOROUGH, W. R. : Some circulatory effects of morphine-barbiturate anesthesia, artificial respiration, and abdominal compression based on ballistocardiographic observations on dogs, with a review of pertinent literature. *American Heart Journal*, 1957, *54:* 5, pp. 651-677

SCARINCI, V. : Azioni farmacologiche del 2-metil-2-*n*-propil-1,3-propandiolo dicarbammato. II (Pharmacological effects of 2-methyl-2-*n*-propyl-1,3-propanediol-dicarbamate. II. Antagonism to morphine. Actions pharmacologiques du méthyl-2-*n*-propyl-2, propanediol-1,3 dicarbamate. II. Antagonisme avec la morphine). *Bollettino della Società Italiana di Biologia Sperimentale*, 1957, *33:* 7, pp. 1165-1167

SCHMIDT-LAMBERG, H. : Morphium : Gutes und Böses (Morphine : Good and bad. Morphine : le bon et le mauvais). *Veska-Zeitschrift*, 1958, *22:* 5, pp. 347-348

SCHAUMANN, W. : Antagonistische Wirkung von Morphin und Cholinesterase-Hemmern auf das Atemzentrum (Antagonistic effects of morphine and cholinesterase antagonists on the respiratory centre. Effets antagonistes de la morphine et des inhibiteurs de la cholinesterase sur le centre respiratoire). *N.-S. Archiv für experimentelle Pathologie und Pharmakologie*, 1958, *233:* 1, pp. 98-111

SCHAUMANN, W. & JOB, C. : Differential effects of a quaternary cholinesterase inhibitor, phospholine, and its tertiary analogue, compound 217-AO, on central control of respiration and on neuromuscular transmission: the antagonism by 217-AO of the respiratory arrest caused by morphine. *Journal of Pharmacology and Experimental Therapeutics*, 1958, *123:* 2, pp. 114-120

SEDLÁCEK, V.; ŠILHAN, J. & KOVARIK, J. : Použiti morfia pri pathologicky prodlouzeném porodu (Use of morphine during pathologically prolonged labour. Emploi de la morphine au cours de l'accouchement pathologique prolongé). *Československá Gynaekologie*, 1957, *22* (36) : 4, pp. 304-309

SHAW, F. H.; GERSHON, S. & BENTLEY, G. A. : Morphine antagonism. *Journal of Pharmacy and Pharmacology*, 1957, *9:* 10, pp. 666-671

SHEER, A. L. : The effect of morphine and other drugs on the peristaltic activity of the guinea pig as measured isometrically in vivo. *Inaug.-Diss. Dokt. Med.*, Bern, 1957, New York, Copley Litho, 1957, In 8°, 22 pp.

SHULMAN, A. & LAYCOCK, G. M. : The analeptic activity of bemegride to structurally unrelated hypnotics. *Australian Journal of experimental Biology and medical Science*, 1957, *35:* 6, pp. 559-568

SIGG, E. B.; CAPRIO, G. & SCHEIDER, J. A. : Synergism of amines and antagonism of reserpine to morphine analgesia. *Proceedings of the Society for experimental Biology and Medicine*, 1958, *97:* 1, pp. 97-100

SINITSYN, L. N. : K voprosu o protivoshokovom deistvii aminazina i mepazina (Problems of anti-shock effects of aminazine and mepazine. Problème des effets anti-choc de l'aminazine et de la mepazine). *Biulleten' eksperimentalnoi Biologii i Meditsiny*, 1958, *45:* 3, pp. 70-72

STEINBERG, S. S.; BELLVILLE, J. W. & SEED, J. C. : The effect of atropine and morphine on respiration. *Journal of Pharmacology and experimental Therapeutics*, 1957, *121:* 1, pp. 71-77

SVENDSEN, A. B. & BERGANE, K. : The quantitative determination of the morphine content of opium by paper chromatography and paper electrophoresis. *Bulletin on Narcotics*, 1958, *10:* 4, pp. 17-19; Dosage de la morphine contenue dans l'opium par la chromatographie sur papier et l'électrophorèse sur papier. *Bulletin des stupéfiants*, 1958, *10:* 4, pp. 18-20

SZERB, J. C. : Interaction of cholinesterase inhibitors with morphine and levallorphan. *Archives internationales de Pharmacodynamie et de Thérapie*, 1957, *111:* 3, pp. 314-321

T

TAKEMORI, A. E. & MANNERING, G. J. : Metabolic N- and O-demethylation of morphine- and morphinan-type analgesics. *Journal of Pharmacology and experimental Therapeutics*, 1958, *123:* 3, pp. 171-179

TAMURA, M. : Studies on sleep and narcosis from the view-point of blood water picture. III. Mechanism of the action of the narcotics and stimulants from the view-point of blood water picture. *Shikoku Acta medica*, 1957, *11:* 1, pp. 62-76

TANABE, T. & CAFRUNY, E. J. : Adrenal hypertrophy in rats treated chronically with morphine. *Journal of Pharmacology and Experimental Therapeutics*, 1958, *122:* 1, pp. 148-153

TANAKA, K. & MISHIMA, H. : The mechanism of antiphlogistic action of morphine. *Yonago Acta medica*, 1957, *2:* 2, pp. 55-59

TAYLOR, H. E.; DOERR, J. C.; GHARIB, A. & FAULCONER Jr., A. : Effect of preanesthetic medication of ether content of arterial blood required for surgical anesthesia. *Anesthesiology*, 1957, *18:* 6, part I, pp. 849-855

V

VALDMAN, A. V. : Vliianie analgetikov na tormozhenie dvigatelno-oboritelnogo uslovnogo refleksa u myshei pri vospalenii vnutrennikh organov (Action of analgesics on inhibition of motor defence conditioned reflexes in mice during inflamatory conditions of the internal organs. L'effet des analgésiques sur l'inhibition du réflexe conditionné de défense moteur chez les souris présentant une inflammation des organes internes). *Farmakologiia i Toksikologiia*, 1957, *20:* 6, pp. 3-9

VALLA, O. A.; DELMAZO, C. A. & GONZALEZ COLOMBO, D. : Desmorfinización brusca por somnoplejía; comentario sobre 1 caso (Abrupt demorphinization by somnoplegia; case report. Démorphinisation brusque par somnoplégie; un cas commenté). *Medicina Panamericana*, 1957, *9:* 11, pp. 571-574

W

* WAKIYAMA, K. : (Pharmacological study of vasomotor centre in cerebral cortex. Etude

pharmacologique du centre vasomoteur dans le cortex cérébral). *Igaku Kenkyu*, 1957, *27:* 9, pp. 2208-2222

WEBER, J. C. : Morphine and amiphenazole for postoperative analgesia following major thoracic surgery. *Journal of Thoracic Surgery*, 1958, *35:* 1, pp. 105-110

WILBRAND, W. : Die Wirkung der Morphinantagonisten auf die Erregbarkeit des Atemzentrums (Effect of morphine antagonists on the irritability of the respiratory center. L'effet des antagonistes de la morphine sur l'excitabilité du centre respitatoire). *Archiv für Gynäkologie*, 1957, *189*, pp. 158-160

WOODS, L. A. : Comparative distribution of morphine and nalorphine in dog brain. *Journal of Pharmacology and experimental Therapeutics*, 1957, *120:* 1, pp. 58-62

C. Other phenanthrene alcaloids and derivatives of opium — Autres alcaloïdes et dérivés phénanthrènes de l'opium

A

ABDEL-RAHMAN, A. A. : Anwendung der Papierchromatographie auf einige Opiumalkaloide und einige Morphinderivate (Application of paper chromatography to some opium alkaloids and morphine derivatives. Application de la chromatographie sur papier à quelques alcaloïdes de l'opium et dérivés de la morphine). *Archiv der Pharmazie und Berichte der Deutschen pharmazeutischen Gesellschaft*, 1957, *290*/62 : 7, pp. 321-325

AXELROD, J. & COCHIN, J. : The inhibitory action of nalorphine on the enzymatic N-demethylation of narcotic drugs. *Journal of Pharmacology and experimental Therapeutics*, 1957, *121:* 1, pp. 107-112

B

BÁNYÁSZ, T. & MARTON, S. : Adatok a dionin tuberkulin-reakciót csökkentő hatásához (Data in the diminishing effect of dionin on tuberculin reaction. Effet diminuant de la dionine sur la réaction à la tuberculine). *Tuberkulózis*, 1957, *19:* 7-9, pp. 188-192

BELLVILLE, J. W.; WALLENSTEIN, S. L.; WALD, G. H.; DOWLING, Jr., M. D. & HOUDE, R. W. : Effect of noscapine and codeine on the respiratory response to carbon dioxide. *Anesthesiology*, 1958, *19:* 4, pp. 545-551

BOGNAR, R. & MAKLEIT, S. : Eine neue Darstellung des Dihydro-6-desoxymorphins (New method for the preparation of dihydro-6-desoxymorphine. Nouvelle synthèse de la dihydro-6-désoxymorphine). *Arzneimittelforschung*, 1958, *8:* 6, pp. 323-325

BORÓN, P. : Badania nad zachowaniem się niektórych reakcji naczynioruchowych w chorobie nadcisnieniowej oraz chorobie wrzodowej żołądka i dwunastnicy I (Behaviour of some unconditioned vasomotor reflexes and the state of reactivity of periphereal vessels to adrenalin and dionin in healthy persons and in neurotic patients. Con portement de certains réflexes vasomoteurs non-conditionnés et état de réactivité des vaisseaux périphériques à l'adrénaline et à la dionine chez l'homme sain et chez le malade nerveux). *Polskie archiwum Medycyny wewnetrznej*, 1958, *28:* 1, pp. 297-312

C

CAHAL, D. A. : Some effects of nalorphine on the behaviour of healthy human volunteers. *Journal of Mental Science*, 1957, *103:* 433, pp. 850-854

D

DELEIXHE, A. & LECOMTE, J. : Intoxication aiguë par l'acédicon; guérison par la nalorphine. *Revue médicale de Liège*, 1958, *13:* 1, pp. 7-9

DELPHAUT, J. & GREGOIRE, H. : Action de l'apomorphine injectée par voie cisternale chez le chien chloralosé. *Comtes rendus des séances de la Société de Biologie et de ses Filiales*, 1957, *151:* 2, pp. 346-348

E

ECKENHOFF, J. E.; HELRICH, M. & ROLPH Jr., W. D. : The effect of dihydrocodeine upon respiration and circulation in man. *Anesthesiology*, 1957, *18:* 6, part I, pp. 891-896

F

FITTKAU, M. & MELZER, W. : Erfahrungsbericht über die Anwendung des Dicodid bei chronischen Lungenleiden (Experimental information on the use of dicodid in chronic lung diseases. Rapport expérimental sur l'emploi du dicodid dans les affections chroniques pulmonaires). *Therapie der Gegenwart*, 1958, 1957, *96:* 12, pp. 457-458

FRASER, H. F.; WIKLER, A.; VAN HORN, G. D.; EISENMAN, Anna J. & ISBELL, H. : Human pharmacology and addiction liability of normorphine. *Journal of Pharmacology and experimental Therapeutics*, 1958, *122:* 3, pp. 359-369

FURRER, W. : Apomorphin-Emetin-Vergällungskur oder Antabus-Stützung? (Apomorphine-emetine denaturation cure or antabus support? L'apomorphine-émétine est-elle une cure de dénaturation ou un adjuvant de l'antabus?) *Praxis*, 1958, *47:* 29, pp. 687-688

G

GIPPERICH, G. : Zur Frage der Wirkung des Morphin-bis-pyridin-3-carbonsäureesters; eines neuen, stark wirkenden Analgetikums (Problem of the effect of morphine-bis-pyridine-3-carbonic acid ester; new long-acting analgesics. Problème de l'effet de la morphine di-(ester de l'acide pyridrique carbonique-3). Nouvel analgésique de longue durée). *Therapeutische Umschau und medizinische Bibliographie*, 1958, *15:* 3, pp. 51-55

GOTO, K. & YAMAMOTO, I. : (+)-metathebainone, (+)-morphothebaine, and thebenine from sinomenine. *Proceedings of the Japanese Academy*, 1958, *34:* 1, pp. 60-63

GROSS, A. : Etude expérimentale, chez le chien chloralosé, de l'action antitussive de la codéine, au moyen du réflexe pleuro-tussigène et de la toux lobélinique. *Comptes rendus des Séances de la Société de Biologie et de ses Filiales*, 1957, *151:* 4, pp. 704-707

GROSS, F. : Erfahrungen mit Ircodenyl in der Ophtalmologie (Experiences with ircodenyl treatment in ophtalmology. Expériences avec l'ircodenyl en ophtalmologie). *Medizinische*, 1957, No. 44, pp. 1267-1268

GRUHZIT, C. C. : Chemoreflex activity of dextromethorphan (romilar), dextrorphan, codeine and morphine in the cat and the dog. *Journal of Pharmacology and experimental Therapeutics*, 1957, *120:* 4, pp. 399-407

H

HADORN, W. : Eine klinische Vorlesung (A clinical lecture. Conférence clinique). *Schweizerische medizinische Wochenschrift*, 1958, *88:* 24, pp. 583-587

HEUERMANN, R. F. & LEVINE, J. : The analysis of combinations of acetylsalicylic acid, acetophenetidin, and caffeine with other drugs. *Journal of the American Pharmaceutical Association, sc. ed.*, 1958, *47:* 4, pp. 276-280

HEUMANN, W. R. : The manufacture of codeine from morphine. *Bulletin on Narcotics*, 1958, *10:* 3, pp. 15-17; La fabrication de la codéine à partir de la morphine. *Bulletin des stupéfiants*, 1958, *10:* 3, pp. 16-18

HOLUBEK, J.; KUDRNÁČ, S. & NOVÁK, M. : Die Bestimmung von Kodein, Narkotin und Thebain in Mohnkapseln (Determination of codeine, narcotine and thebaine in poppy-heads. Titration de codéine, narcotine et thébaine dans la tête de pavot). *Pharmazie*, 1958, *13:* 2, pp. 95-99

K

KASE, Y.; YUIZONO, T.; SERIKAWA, H.; YAMAMOTO, S.; YAMASAKI, T.; FUSHIMIZU, T.; KATAYAMA, N.; MORIYA, T. & NOZUHARA, T. : d-3-dimethylamino-1,1-diphenylbutyl ethyl sulfone as a long-acting antitussive. *Chemical and Pharmaceutical Bulletin of Japan*, 1958, *6:* 1, pp. 109-111

KEATS, A. S.; TELFORD, J. & KUROSU, Y.: Studies on analgesic drugs: dihydrocodeine. *Journal of Pharmacology and experimental Therapeutics*, 1957, *120:* 3, pp. 354-360

KELENTEY, B.; CZOLLNER, F.; STENSZKY, E.; MÉSZÁROS, Z. & SZLÁVIK, L.: Darstellung und pharmakologische Untersuchung einiger morpholylaethylisierter Morphin-Derivate (Preparation and pharmacological examination of some morpholylethylized morphine derivatives. Préparation et étude pharmacologique de quelques dérivés morpholyléthyle de la morphine). *Arzneimittelforschung*, 1958, *8:* 6, pp. 325-330

KELENTEY, B.; STENSZKY E.; CZOLLNER, F.; MÉSZÁROS, Z. & SZLÁVIK, L. : Az acetylezett morphinszármazékok pharmacológiai vizsgálata (Pharmacological study of acetylated morphine derivatives. Etude pharmacologique de dérivés acétylés de la morphine). *Kisérletes orvostudomány*, 1958, *10:* 1, pp. 25-35

KELENTEY, B.; STENSZKY, E.; CZOLLNER, F.; MÉSZÁROS, Z. & SZLÁVIK, L. : Darstellung und pharmakologisches Verhalten von Morphinderivaten I (Preparation and pharmacological action of morphine derivate. I. Préparation et action pharmacologique des dérivés de la morphine. I). *Pharmazie*, 1957, *12:* 9, pp. 600-607

L

* LABENSKIJ, A. S. : (Narcotoline from opium. La narcotoline de l'opium). *Zhurnal prikladnoi Khimii SSSR*, 1958, *31:* 2, pp. 323-324

LOCKETT, M. F. & DAVIS, M. M. : The analgesic action of normorphine administered intracisternally to mice. *Journal of Pharmacy and Pharmacology*, 1958, *10:* 2, pp. 80-85

LURIA, E. : Dapatazol and megimide in dicodid, barbiturate and largactil poisoning. *Harefuah*, 1956, *51:* 8, pp. 188-189

M

MAURATH, J. & RÜGER, R. : Kann die atemdepressive Wirkung des Morphiums durch Allyl-Derivate des Morphins verhindert werden? (Can the allyl derivates of morphine prevent its respiratory depressant action? L'action dépressive respiratoire de la morphine peut-elle être inhibée par les dérivés allyliques de la morphine?) *Arzneimittel-Forschung*, 1957, *7:* 11, pp. 665-672

MISZKE, A. : O zastosowaniu skopodalu do znieczulenia podstawowego w zabiegach otorino-laryngologicznych (Application of scopodal for basic anesthetic in otorinolaryngological surgery. Usage de scopodal comme anesthésique de base en chirurgie oto-rhinolaryngologique). *Otolaryngologia polska*, 1957, *11:* 2, pp. 187-190

MYERS, J. D. : A preliminary clinical evaluation of dihydrocodeine bitartrate in normal parturition. *American Journal of Obstetrics and Gynecology*, 1958, *75:* 5, pp. 1096-1100

P

PADOAN, A. : Esperienze cliniche con un nuovo analgesico in chirurgia infantile (Clinical tests of a new analgesic in infantile surgery. Essais cliniques d'un nouvel analgésique en chirurgie infantile). *Minerva Pediatrica*, 1958, *10:* 19-20, pp. 569-571

PEENEN, P. F. D., van & WAY, A. L. : The effect of certain central nervous system depressants on pituitary-adrenali activating agents. *Journal of Pharmacology and experimental Therapeutics*, 1957, *120:* 2, pp. 261-267

PINGUET : Application de l'alcoolyse au dosage de quelques médicaments acétylés. *Pharmaceutica Acta Helvetiae*, 1958, *33:* 3, pp. 114-119

R

RASMUSSEN, H. B.; BERGER, J.; FOLTING, K. & ESPERSEN, G. : Identifikation af laegemidler. V. Analgetika fra morphingruppen (Identification of drugs. V. Analgesics from the morphine group. Identification de médicaments. V. Analgésiques du groupe de la morphine). *Dansk Tidsskrift for Farmaci*, 1958, *32:* 4, pp. 81-88

ROSENKILDE, H. & GOVIER, W. M. : A comparison of some phenothiazine derivatives in inhibiting apomorphine-induced emesis. *Journal of Pharmacology and experimental Therapeutics*, 1957, *120:* 3, pp. 375-378

RUCH, W. A. & RUCH, R. M. : A preliminary report on dihydrocodeine-scopolamine in obstetrics. *American Journal of Obstetrics and Gynecology*, 1957, *74:* 5, pp. 1125-1127

S

SCHMIDT, R. : Zur Schmerzlinderung mit Ircodenyl in der Chirurgie (Analgesia with ircodenyl in surgery. Analgésie par l'ircodenyl en chirurgie). *Therapie der Gegenwart*, 1957, *96:* 10, pp. 382-383

SKURSKY, J. : Erfahrungen über die schmerzstillende Wirkung mit einem stark wirksamen neuen Analgetikum (Experiences with a very effective new analgesic. Expériences avec un nouvel analgésique très puissant). *Wiener medizinische Wochenschrift*, 1957, *107:* 32-33, pp. 678-679

STRAND, H. A.; HENNINGER, F. & DILLE, J. M. : Evaluation of analgetic combinations for dental use. *Journal of the American Dental Association*, 1958, *56:* 4, pp. 491-498

T

TABORSKY, L. : Ueber die Behandlung einer Pantoponvergiftung mit dem Morphinantagonisten Allylderivat Ro l-7700 (Treatment of pantopon poisoning with a morphine antagonist allylderivative, Ro l-7700. Traitement d'un empoisonnement au pantopon par un dérivé allylique et antagoniste de la morphine, Ro l-7700). *Wiener medizidinische Wochenschrift*, 1958, *108:* 10, pp. 220-221

TADDEI, I. & TIEZZI, C. : La cloropromazina (largactil) facilita nel gatto il vomito da apomorfina (Chlorpromazine (largactil) facilitates vomiting induced by apomorphine in cats. La chlorpromazine (largactil) facilite les vomissements provoqués par l'apomorphine chez le chat). *Atti dell'Accademia dei fisiocritici in Siena*, sezione medico-fisica, 1957, vol. 4, pp. xlvi-li

TAKAGI, K.; FUKUDA, H. & YANO, K. : Antitussive activity of the N-oxides of opium alkaloids. *Journal of the Pharmaceutical Society of Japan*, 1957, *77:* 12, p. 1358

TOLBERT, B. M. : Estimated radiation dosage in man from administered morphine-N-methyl-C14. *University of California Radiation Laboratory*, 1957, UCRL-3806, pp. 1-7

TOWSEND Jr., E. H. : Prolonged cough suppression. *New England Journal of Medicine*, 1958, *258:* 2, pp. 63-67

V

VIDIC, E. : Ein neues Reagens zur Unterscheidung von Morphinderivaten (A new reagent for the determination of morphine derivatives. Un nouveau réactif pour la détermination des dérivés de la morphine). *Archiv für Toxikologie; Fühner-Wielands Sammlung von Vergiftungsfällen*, 1957, *16:* 6, pp. 412-418

W

WILNER, D. M.; ROSENFELD, E.; LEE, R. S.; GERARD, D. L. & CHEIN, I. : Heroin use and street gangs. *Journal of criminal law, Criminology and Police science*, 1957, *48:* 4, pp. 399-409

WOODS, L. A. & MUEHLENBECK, H. E. : Distribution and fate of nalorphine in the dog and rat. *Journal of Pharmacology and experimental Therapeutics*, 1957, *120:* 1, pp. 52-57

D. Other drugs and substances derived from the opium poppy — Autres drogues et substances dérivées du pavot à opium

A

AWE, W. & WINKLER, W. : The alkaloids of the common poppy and the opium alkaloid porphyroxine. *Bulletin on Narcotics*, 1958, *10:* 4, pp. 20-29; Les alcaloïdes du pavot commun et l'alcaloïde de l'opium dénommé porphyroxine. *Bulletin des stupéfiants*, 1958, *10:* 4, pp. 21-24

AXELROD, J. & INSCOE, J. K. : (3'-Methoxy-4'-hydroxybenzyl) 6-7-dimethoxy isoquinoline, a major metabolite of papaverine. *Experientia*, 1957, *13:* 8, pp. 319-320

B

BERGE, B. S. TEN & ASSEN, F. J., VAN. : Diabetes und Schwangerschaft : Geburtseinleitung mit Compositrin (Diabetes mellitus and pregnancy: labor induction with compositrin. Diabète et grossesse. Amorçage de l'accouchement par la compositrin). *Archiv für Gynäkologie*, 1957, *189*, pp. 189-191

C

CAVALLINI, L. : Attività terapeutica del teofillinato di collina associato al tricloro-ossietil-paramimobenzoato di papaverina (Therapeutic activity of choline theophyllinate associated with papaverine trichlorhydroxyethyl-p-aminobenzoate. Activité thérapeutique du theophyllinate de choline associé au trichlorhydroxyethyl p-aminobenzoate de papaverine). *Minerva médica*, 1958, *49:* 19, pp. 805-809

COBBIN, L. B. & THORP, R. H. : The spasmolytic actions of some synthetic compounds related to papaverine. *Australian Journal of experimental Biology and Medical Science*, 1957, *35:* 3, pp. 249-255

D

DAMIANOVICH, J. : La emetina y el láudano en la práctica pediátrica (Emetine and laudanum in pediatric practice. Emétine et laudanum en pédiatrie). *Revista de la Asociación Médica Argentina*, 1957, *71:* 8, pp. 266-269

DELTOMBE, J. & LEBOUTTE, G. : Les méthodes de dosage de l'amylocaïne. *Journal de Pharmacie de Belgique*, 1958, *40:* 1-2, pp. 38-43

DENNEMARK, H. G. : Die medikamentöse Behandlung nervöser Rhytmusstörungen, insbesondere des Dies inversus (Medical treatment of nervous rhythm disorders, especially dies inversus. Traitement médicamenteux des désordres nerveux du rhytme, en particulier du dies inversus). *Medizinische*, 1958, No. 25, pp. 1033-1034

DESCUNS, P.; GARRÉ, H. & ENJALBERT, J. M. : L'injection carotidienne de papavérine dans les spasmes vasculaires cérébraux. *Revue d'Oto-Neuro-Ophtalmologie*, 1957, *29:* 2, pp. 123-125

E

ENDERS, A. & SCHMIDT, L. : Die reflektorische Tätigkeit des Husten- und Atemzentrums unter dem Einfluss von Papaverinhydrochlorid (Reflex activity of the cough centre and the respiratory centre under the influence of papaverin hydrochloride. Activité réflexe des centres de la toux et respiratoire sous l'influence de chlorhydrate de papavérine). *Archives internationales de Pharmacodynamie et de Thérapie*, 1958, *114:* 3-4, pp. 446-450

ERVENIUS, O. : Narkotin som hosthämmande medel (Narcotine as a cough inhibitor. La narcotine comme inhibiteur de la toux). *Svensk farmaceutisk Tidskrift*, 1957, *61:* 28, pp. 773-776

G

GIOTTI, A. & PEPEU, G. : Interazioni fra A.T.P. e papaverina a livello cardiaco (Interactions between adenylpyrophosphate and papaverine at the cardiac level. Interaction entre le phosphate pyrique d'adenyl et la papaverine au niveau du cœur). *Bollettino della Società italiana di Biologia sperimentale*, 1958, *34:* 9, pp. 449-452

H

HARLACHER, A. : Beitrag zur postoperativen Anwendung des Spasmolytikums Parinokhellin in der Thoraxchirurgie (Postoperative use of the spasmolytic parinokhellin in thoracic surgery. Emploi post-opératoire du spasmolytique parinokhellin en chirurgie thoracique). *Muenchener medizinische Wochenschrift*, 1957, *99:* 34, pp. 1207-1208

HELGREN, P. F.; CHADDE, F. E. & CAMPBELL, D. J. : The determination of theophylline, pentobarbital, and papaverine in tablets by spectrophotometric analysis. *Journal of the American Pharmaceutical Association; Scientific Edition*, 1957, *46: 11*, pp. 644-646

HOLUBEK, J.; KUDRNÁČ, S. & NOVÁK, M. : Die Bestimmung von Kodein, Narkotin und Thebain in Mohnkapseln (Determination of codeine, narcotine and thebaine in poppy head. Titration de codéine, narcotine et thébaïne dans la tête de pavot). *Pharmazie*, 1958, *13:* 2, pp. 95-99

K

KISIN, I. E. : Vliianie papaverina i dibazolana skorost koronarnogo krovoobrashcheniia (Effect of papaverine and dibazol on coronary circulation rate. Effet de la papavérine et du dibazol sur le taux de la circulation coronaire). *Biulleten Experimental'noi Biologii i Meditsiny*, 1958, *45:* 6, pp. 69-72

* KREPINSKI, J. : (Polarographic determination of Papaveraldine. Détermination polarographique de la papaveraldine). *Ceskoslovenska Farmaci*, 1958, 7, p. 13

L

LEE, K. T. & FARMILO, C. G. : Determination of papaverine and narcotine by using ammonium reinackate. *Nature*, 1957, *180:* 4597, pp. 1288-1289

LEE, K. T. & FARMILO, C. G. : The quantitative separation of papaverine from narcotine in mixtures. *Journal of Pharmacy and Pharmacology*, 1958, *10:* 7, pp. 427-435

LU, F. C. : A comparative study on the coronary dilator activity of aminophylline and papaverine. *Revue Canadienne de Biologie*, 1957, *16:* 3, pp. 390-393

M

MACRIS, S. G.; GRAVENSTEIN, J. S.; REICHLE, C. W. & BEECHER, H. K. : Drug synergism (potentiation) in pain relief in man: papaverine and morphine. *Science*, 1958, *128:* 3315, pp. 84-85

MACRIS, S. G.; SMITH, G. M. & BEECHER, H. K. : Comparison of the antipruritic effect of morphine and papaverine in experimental and pathological itch in man. *Journal of Pharmacology and experimental Therapeutics*, 1958, *123:* 3, pp. 220-223

MAGALDI, R. : Contributo sperimentale alla interpretazione del meccanismo d'azione della β-mercaptoetilamina nella prevenzione del vomito postoperatorio (Interpretation of the mechanism of action of β-mercapto-ethylamine in prevention of postoperative vomiting. Contribution expérimentale à l'interprétation du mécanisme d'action de la β-mercaptoéthylamine dans la prévention des vomissements post-opératoires). *Atti dell'Accademia dei Fisiocritici in Siena, sezione medico-fisica*, 1957, vol. 4, pp. 85-89

MENGE, H. G. : Der Einfluss von Khellin und seiner Kombination mit Papaverin auf die Gehirndurchblutung (Effect of khellin and its combination with papaverine on brain blood supply. Action de la khelline et de sa combinaison avec la papavérine sur l'apport sanguin au cerveau). *Medizinische Klinik*, 1957, *52:* 51, pp. 2204-2206

P

PINAR MARTINEZ, M. : Aportación en la síntesis de la papaverina. I. Síntesis a partir de azlactonas (Contribution to the synthesis of papaverine. I. Synthesis from azlactonas. Contribution à la synthèse de la papavérine. I. Synthèse à partir d'azlactones). *Anales de la Real Academia de Farmacia*, 1957, *23:* 4, pp. 387-392

* POZDNJAKOVA, V. T. : (Styphnic acid as reagent in micro-crystalloscopic and crystalloptic research on alkaloids. L'acide styphnique comme réactif pour la recherche microcristalloscopique et cristalloptique des alcaloïdes). *Ukrainskii khimicheskii Zhurnal*, 1957, *23:* 6, pp. 777-783

R

ROSENKILDE, H. & GOVIER, W. M. : A comparison of some phenothiazine derivatives in inhibiting apomorphine-induced emesis. *Journal of Pharmacology and experimental Therapeutics*, 1957, *120:* 3, pp. 375-378

S

SCHIFIS, M. & BASTAROLI, J. C. : Ensayo clínico de la Rauwolfia, bromuro de bromocalina, y clorhidrato de papaverina combinados, en el tratamiento de la hipertensión arterial (Clinical tests of combined Rauwolfia, bromocholine bromide and papaverine hydrochloride in the treatment of arterial hypertension. Essais cliniques de Rauwolfia, bromure de bromocholine et chlorhydrate de papavérine combinés, dans le traitement de l'hypertension artérielle). *Día médica* (B.A.), 1958, *30:* 33, p. 1151; passim

SEGAL, M. S.; GOLDSTEIN, M. M. & ATTINGER, E. O. : The use of noscapine (narcotine) as an antitussive agent. *Diseases of the Chest*, 1957, *32:* 3, pp. 305-309

SETNIKAR, I.; TEMELCOU, O. & BIANCHI, C. : Caracteristiche farmacologiche del 4-cloro-3-aminobenzoato di dimetilamino etile (Rec 1-0060) (Pharmacological characteristics of dimethylamino ethyl 4-chlor-3-aminobenzoate. Caractéristiques pharmacologiques du chloro-4 aminobenzoate-3 d'éthyl diméthylamine). *Bollettino chimico farmaceutico*, 1958, *97:* 8, pp. 457-480

SOMMARIVA, V. & RAPISARDA, L. M. : Modificazioni del quadro elettroforetico delle lipo-glico-sieroproteine arteriose e venose distrettuali in sogetti aeteriopatici dopo trattamento con cocktail farmacologico (Changes in the electrophoretic picture of lipoproteines and glycoprotein fractions in arterial and venous blood of patients of arterial diseases after drug cocktail therapy. Modification de l'image électrophorétique de fragments de lipoprotéines et glucoprotéines dans le sang artériel et veineux de sujets artériopathes après traitement par cocktail pharmacologique). *Rivista di Patologia e Clinica*, 1958, *13:* 2, pp. 41-61

STOLL, P. : Zur Behandlung von Schmerzzuständen im kleinen Becken der Frau mit Ichtobellol compositum (Treatment of painful conditions in the true pelvis of the female with ichtobellol compositum. Douleurs du pelvis de la femme traitées avec l'Ichtobellol compositum). *Medizinische Klinik*, 1957, *52:* 41, pp. 1800-1801

STREIT, M. & TAESCHLER, M. : Pharmacodynamische Untersuchungen am experimentellen Herzinfarkt der Ratte (Pharmacodynamic studies on experimental cardiac infarcts in

rats. Recherches pharmacodynamiques sur l'infarct cardiaque expérimental chez le rat). *Acta Physiologica et Pharmacologica Neerlandica*, 1957, vol. *6*, pp. 27-34

W

WEAVER, L. C.; ALEXANDER, W. M.; ABREU, B. E.; RICHARDS, A. B.; JONES, W. R. & BEGLEY, R. W. : The mechanism of the hypotensive action of narcotine hydrochloride. *Journal of Pharmacology and experimental Therapeutics*, 1958, *123:* 4, pp. 287-295

WACHSMUTH, H. & CORNELIS, K. : Réactions colorimétrique et fluorimétrique de la papavérine. *Journal de Pharmacie de Belgique*, 1958, *13:* 3-4, pp. 130-134

Part III. — THE COCA LEAF AND COCAINE — LA FEUILLE DE COCA ET LA COCAINE

A

ADRIANI, J. & CAMPBELL, D. : The absorption of topically applied tetracaine and cocaine. *Laryngoscope*, 1958, *68:* 1, pp. 65-72

C

CHOPRA, I. C. & CHOPRA, R. N. : The cocaine problem in India. *Bulletin on Narcotics*, 1958, *10:* 2, pp. 12-24; La question de la cocaïne en Inde. *Bulletin des stupéfiants*, 1958, *10:* 2, pp. 12-24

D

DELPHAUT, J. & LANZA, M. : Action de quelques médicaments ataraxiques sur l'agitation provoquée chez la souris blanche par l'amphétamine et la cocaïne. *Journal de Physiologie*, 1958, *50:* 2, pp. 250-251

DELTOMBE, J. & LEBOUTTE, G. : Les méthodes de dosage de l'amylocaïne. *Journal de Pharmacie de Belgique*, 1958, *40:* 1-2, pp. 38-43

H

HAMMOND, P. V. : Studies on the effects of ephedrine in the presence of cocaine. *Journal of the American pharmaceutical association*, scient. ed., 1958, *47:* 1, pp. 67-69

HERR, F. : Zur Frage der Standardisierung der Prüfung von Lokalanästhetica (Standardization problem of local anaesthetics assay. Le problème de la standardisation des essais des anesthésiques locaux). *Arzneimittel-Forschung*, 1958, *8:* 3, pp. 137-141

HERR, F. & BALOGH, J. : Prüfung des Diffusionsvermögens einiger Lokalanaesthetica (Assay of diffusion power of some local anaesthetics. Essai du pouvoir de diffusion de quelques anesthésiques locaux). *Archiv für experimentelle Pathologie und Pharmakologie*, 1957, *232:* 1, pp. 305-306

HORITA, A. : A vasopressor response to reserpine in the cocainized dog. *Journal of Pharmacology and experimental Therapeutics*, 1958, *122:* 4, pp. 474-479

K

KADLECOVÁ, V. & PELEŠKA, M. : Infraskopická studie. VI. Učinek kokainu na zornici v závislosti na věku sledovaný infraskopicky (Infrascopic studies. VI. Effect of cocaine on the pupil and its dependence on age as revealed by infrascopic studies. Etudes infrascopiques. VI. Effet de la cocaïne sur la pupille, dépendant de l'âge (du sujet) comme le révèle l'infrascopie). *Československa ofthalmologie*, 1958, *14:* 3, pp. 168-173

KOBINGER, W. : Differentiation between the sedative actions of 5-hydroxytryptamine and reserpine in mice by means of two stimulating substances. *Acta Pharmacologica et Toxicologica*, 1958, *14:* 2, pp. 138-147

L

LAROCHE, M. J. & QUEVAUVILLER, A. : Comparaison de l'activité anesthésique locale d'infiltration du chlorhydrate de cocaïne chez le cobaye tuberculeux et le cobaye normal. *Anesthésie, Analgésie, Réanimation*, 1958, *15:* 1, pp. 116-119

P

* POZDNJAKOVA, V. T. : (Styphnic acid as reagent in micro-crystalloscopic and crystalloptic research on alkaloids. L'acide styphnique comme réactif pour la recherche microcristalloscopique et cristalloptique des alcaloïdes). *Ukrainskii khimicheskii Zhurnal*, 1957, *23:* 6, pp. 777-783

T

TADDEI, I. & IAPPINI, M. : Osservazioni farmacologiche sull'azione dell'apomorfina, esetone e cocaina nell'animale ipocalcemico (Pharmacological observations on the effect of apomorphine, esetone and cocaine in the hypocalcemic animal. Observations pharmacologiques sur l'action de l'apomorphine, de l'esetone et de la cocaïne sur l'animal hypocalcemique). *Archivio Italiano di Scienze Farmacologiche*, 1957, *7:* 3, pp. 194-205

W

WOODS, L. A. & HAGGART, J. : Apneic and hypotensive effects of local anesthetic drugs in dogs and mice under general anesthesia. *Anesthesiology*, 1957, *18:* 6, part I, pp. 831-840

WUERFLER, P. : Selbstblendung eines cocainsüchtigen Betrugers (Self-blinding by a cocaine addicted imposter. Un imposteur cocaïnomane se rend aveugle). *Nervenarzt*, 1956, *27*, pp. 325-326

Z

ZETLER, G. & MOOG, E. : Die Bulbocapnin-Katatonie, ihre Synergisten und Antagonisten (Bulbocapnine catatonia, its synergists and antagonists. Synergie et antagonisme de la catatonie provoquée par la bulbocapnine). *Archiv für experimentelle Pathologie und Pharmakologie*, 1958, *232:* 2, pp. 442-458

ZLOTNIKOV, S. A. : O vliianii kokaina na vestibuliarnye refleksy; eksperimental'nye issledovaniia (Effect of cocaine on vestibular reflexes; experimental research. Action de la cocaïne sur les réflexes vestibulaires; Recherche expérimentale). *Vestnik Oto-Rino-Laringologii*, 1957, *19:* 3, pp. 68-71

Part IV. — CANNABIS AND ITS DERIVATIVES — LE CANNABIS ET SES DÉRIVÉS

A

AMES, F. : A clinical and metabolic study of acute intoxication with *Cannabis sativa* and its role in the model psychoses. *Journal of mental sciences*, 1958, *104:* 437, pp. 972-999

B

BENABUD, A. : Psycho-pathological aspects of the cannabis situation in Morocco: statistical data for 1956. *Bulletin on Narcotics*, 1957, *9:* 4, pp. 1-16; Aspects psychopathologiques du cannabisme au Maroc; données statistiques pour l'année 1956. *Bulletin des stupéfiants*, 1957, *9:* 4, pp. 1-17

F

FERENCZY, L.; GRACZA, L. & JAKOBEY, I. : An antibacterial preparatum from Hemp (Cannabis Sativa L.). *Naturwissenschaften*, 1958, *45:* 8, p. 188

K

KABELIK, J. : Hanf (Cannabis sativa), antibiotisches Heilmittel. I. Hanf in der Alt- und Volksmedizin (Hemp (Cannabis sativa) antibiotic drug. I. Hemp in the old and popular medicine. Le chanvre (Cannabis sativa) drogue antibiotique. I. Le chanvre dans la médecine ancienne et populaire). *Pharmazie*, 1957, *12:* 7, pp. 439-443

KREJČI, Z. : Hanf (Cannabis sativa) — Antibiotisches Heilmittel. II. Methodik und Ergebnisse der bakteriologischen Untersuchungen und vorläufige klinische Erfahrungen (Hemp (Cannabis sativa) — antibiotic drugs. II. Method and results of bacteriological experiments and preliminary clinical experience. Chanvre (Cannabis sativa) — substances antibiotiques. II. Méthode et résultats des recherches bactériologiques et d'expériences cliniques préliminaires). *Die Pharmazie*, 1958, *13:* 3, pp. 155-166

Part V. — SYNTHETIC DRUGS — STUPÉFIANTS SYNTHÉTIQUES

A. General Works — Généralités

B

BEASLEY, Y. M.; PETROW, V. & STEPHENSON, O. : Analgesics. I. Some aryloxypropanolamines. *Journal of Pharmacy and Pharmacology*, 1958, *10:* 1, pp. 47-59

E

EDDY, N. B.; HALBACH, H. & BRAENDEN, O. J. : Synthetic substances with morphine-like effect; clinical experience; potency, side-effect, addiction-liability. *Bulletin of the WHO*, 1957, *17:* 4-5, pp. 569-863

F

FISCHER, R. & OTTERBECK, N. : Zum Nachweis von Analgeticis (Opium-Alkaloiden, deren Derivaten und synthetischen Substanzen) mittels "Test-Tube" — Chromatographie (Test-tube chromatography in determination of analgesics. (Opium alkaloids, derivatives and synthetic substances). Mise en évidence d'analgésiques (alcaloïdes de l'opium, leurs dérivés et substances synthétiques) au moyen de la microchromatographie (tube-test). *Scientia pharmaceutica*, 1957, *25:* 4, pp. 242-248

FOLDES, F. F.; DUNCALF, D.; ROBBINS, R. S.; D'SOUSA, P. B. & CONTE, A. A. : Production of controllable annea in anesthesia; combined use of narcotic analgesics and their antagonists. *Journal of the American Medical Association*, 1958, *166:* 4, pp. 325-331

H

HACH, V. & HACH, E. : Fortschritte auf dem Gebiet der Arzneimittelsynthese im Jahre 1956 (Developments in the field of drug synthesis in 1956. Progrès dans le domaine des drogues synthétiques en 1956). *Pharmazie*, 1957, *12:* 12, pp. 781-794

HENECKA, H. : Versuche zur Synthese von Substanzen mit Morphinwirkung (Attempted synthesis of morphine-like substances. Essai de synthèse de substances d'action morphinique). *Medizin und Chemie*, 1953, III, pp. 403-407

J

JACOB, J.; BLOZOVSKI, M. & ECHINARD-GARIN, P. : Propriétés analgésiques de quatre amino - méthyl - 2 - benzoyl - 7 - benzodioxans. *Thérapie, 13:* 1, pp. 17-29

K

KASE, Y. *et al* : d-3-dimethylamino-1, l-diphenylbutyl ethyl sulfone as a long-acting antitussive, *Chemical and pharmaceutical Bulletin of Japan*, 1958, *6:* 1, pp. 109-111

KHARKEVICH, D. A. : O kombinirovannom deistvii displatsina i narkotikov (Combined effect of displacin and narcotics. Action combinée de la displacin avec des narcotiques). *Farmakologiia i Toksikologiia*, 1958, *21:* 3, pp. 12-17

M

MEDAKOVIC, M. : Comparisons of antagonistic potencies of morphine-like analgesics towards 5-hydroxytryptamine on the guinea pig ileum. *Archives internationales de Pharmacodynamie et de Thérapie*, 1958, *114:* 2, pp. 201-209

S

SCHIFFRIN, M. J. & SADOVE, M. S. : Synthetic narcotic analgetics and their antagonists. *G. P.*, 1958, *17:* 2, pp. 106-114

* SUGIMOTO, N. & SHIGEMATSU, N. : (Study on synthetic analgesics. XI. Etudes sur les analgésiques synthétiques. XI.) *Journal of Pharmacy of the Society of Japan*, 1957, *77:* 8, pp. 927-928; XII., *ibid.*, pp. 929-930

T

TANCREDI, G. : Il problema degli stupefacenti sintetici (Problem of synthetic narcotics. Le problème des stupéfiants de synthèse). *Minerva Farmaceutica*, 1957, *6:* 5, pp. 98-100

B. Pethidine and related compounds — Péthidine et composés apparentés

A

ANONYMOUS — ANONYME : Anileridine hydrochloride. *Journal of the American Medical Association*, 1958, *197:* 1, pp. 62-63; Anileridine phosphate, *ibid.*, pp. 63-64

ANONYMOUS — ANONYME : Supplemental anesthesia; a simple technique for cataract surgery. *Connecticut State medical Journal*, 1958, *22:* 3, pp. 173-174

B

BATTERMAN, R. C.; GOLBEY, M.; GROSSMAN, A. J. & LEIFER, P. : Analgesic effectiveness of orally administered ethoheptazine in man. *American Journal of the medical Sciences*, 1957, *234:* 4, pp. 413-419

BECKETT, A. H.; CASY, A. F.; KIRK, G. & WALKER, J. : Alpha- and beta-prodine type compounds : configurational studies. *Journal of Pharmacy and Pharmacology*, 1957, *9:* 12, pp. 939-948; discussion, pp. 948-949

C

CARLSON, V. R. : Individual pupillary reactions to centrally-acting drugs in man. *Journal of Pharmacology and experimental Therapeutics*, 1957, *121:* 4, pp. 501-506

CASS, L. J.; FREDERIK, W. S. & BARTHOLOMAY, A. F. : Methods in evaluating ethoheptazine and ethoheptazine combined with aspirin. *Journal of the American Medical Association*, 1958, *166:* 15, pp. 1829-1833

CHANG, F. F.; SAFAR, P. & LASAGNA, L. : Narcotic potency and side effects of anileridine and meperidine in man. *Journal of Pharmacology and experimental Therapeutics*, 1958, *122:* 3, pp. 370-378

CLIFFORD, D. H. : Effect of preanesthetic medication with chlorpromazine, meperidine and promazine on pentobarbital anesthesia in the cat. *Journal of the American Veterinary Medical Association*, 1957, *131:* 7, pp. 415-419

D

DECHENE, J. P. & HOULD, R. : Anesthésie potentialisée et nisentil en chirurgie thoracique. *Laval médical*, 1957, *24:* 3, pp. 307-320

DMOCHOWSKI, J. : Wpływ morfiny i dolantyny na czynność oddechową w zależności od dużych dawek largaktylu (Effect of large doses of largactil on respiratory reactions to morphine and dolantin. Action du largactil en hautes doses sur les réactions respiratoires à la morphine et la dolantine). *Acta Physiologica polonica*, 1957, *8:* 3-3a, pp. 311-312

DODIS, A. : Emploi de l'alphaprodine comme analgésique en chirurgie et en médecine. *Union médicale du Canada*, 1957, *86:* 10, pp. 1103-1108

DRIPPS, R. D.; MILLAR, R. A. & KNEALE, D. H. : A comparison of anileridine, morphine and meperidine in man. *Surgery, Gynecology and Obstetrics*, 1957, *105:* 3, pp. 322-326

F

FISCHMAN, M.; RIVKIND, G. & NAOM, L. : Analgesia con merperidina para esofagoscopia (Meperidine analgesia in esophagoscopy. Analgésie à la mépéridine en esophagoscopie). *Prensa médica argentina*, 1958, *45:* 2, pp. 221-224

FOLDES, F. F. & ERGIN, K. H. : Levallorphan and meperidine in anesthesia; study of effects in supplementation of nitrous oxide-oxygen-thiopental sodium anesthesia. *Journal of the American Medical Association*, 1958, *166:* 12, pp. 1453-1458

G

GIBNEY, P. & LOVERME, S. : A new use for promethazine hydrochloride. *Anesthesiology*, 1958, *19:* 3, pp. 402-403

GILLIAM, J. S.; HUNTER, G. W.; DARNER, C. B. & THOMPSON, G. R. : Meperidine hydrochloride and alphaprodine hydrochloride as obstetric analgesic agents; a double-blind study. *American Journal of Obstetrics and Gynecology*, 1958, *75:* 5, pp. 1105-1110

GROSS, S. J.; KATOH, J. & MAECK, J. V. : Anileridine analgesia in labor. *Journal of the Maine Medical Association*, 1958, *49:* 5, pp. 174-176

GROSSMANN, V. : Vliv záření na schopnost jaterní tkáně rozkládat dolsin (Effect of radiations on dolsin-decomposing capacity of the liver tissue. Effet des radiations sur la capacité du tissu hépathique de décomposer la dolsin). *Československá Fysiologie*, 1958, *7:* 1, p. 145

GUERNSEY, L. H. : Bilateral forward dislocation of the mandibular condyles in open position; a method of reduction using anectine. *Medical Bulletin of the U.S. Army, Europe*, 1958, *15:* 3, pp. 57-59

H

HAID, B. : 8 Tetanusfälle innerhalb eines Jahres; 7 davon geheilt entlassen (Eight cases of tetanus within a year, seven cured. Huit cas de tétanos en un an, sept guéris). *Anaesthesist*, 1958, *7:* 4, pp. 105-107

HARRIS, H.; TAFEEN, C. H.; FREEDMAN, H. L. & FOGARTY, E. : The intravenous use of demerol, scopolamine and nalline in labor. *American Journal of Obstetrics and Gynecology*, 1958, *75:* 1, pp. 39-42

HAYWARD-BUTT, J. T. : Ataralgesia. Operations without anaesthesia. *Lancet*, 1957, *7003*, pp. 972-974

HERXHEIMER, A. & SANGER, C. : Analgesic action of pethidine-levallorphan mixtures in man. *British Medical Journal*, 1957, No. *5048*, pp. 802-803

HOLMES, J. M. : Morpholinoethylnorpethidine hydrochloride in obstetrics. *Journal of Obstetrics and Gynecology of the British Empire*, 1958, *65:* 1, pp. 98-99

HU, T. T. : Intravenous procaine-meperidine anesthesia. *Chinese Journal of Surgery*, 1957, *5:* 8, pp. 644-648, English abstract, pp. 79-80

J

JANSSEN, P. A. J. & JAGENEAU, A. H. : A new series of potent analgesics : dextro 2:2-diphenyl-3-methyl-4-morpholinobutyryl-pyrrolidine and related basic amides. II. Comparative analgesic activity, acute toxicity and tolerance development in rats for R 875, morphine, pethidine and methadone. *Journal of Pharmacy and Pharmacology*, 1958, *10:* 1, pp. 14-21

K

KEATS, A. S.; TELFORD, J. & KUROSU, Y. : Studies of analgesic drugs : anileridine dihydrochloride. *Anesthesiology*, 1957, *18:* 5, pp. 690-697

KLEIN, M. R. & DELÈGUE, L. : Erfahrungen mit Neurolytika bei neurochirurgischen Eingriffen im Kindersalter (Tests of neurolytic drugs in neurosurgical operations in children. Expériences avec les neurolytiques en neurochirurgie infantile). *Deutsche medizinische Wochenschrift*, 1957, *82:* 38, pp. 1654-1656

KOPF, R. & MØLLER NIELSEN I. : Pharmacology and toxicology of captodiamine (p-butylmercapto-benzhydryl-β-dimethylamino-ethylsulphide). *Arzneimittel-Forschung*, 1958, *8:* 3, pp. 154-159

L

LAMB, H. : The use of nisentil in general practice. *Journal of the Michigan State Medical Society*, 1958, *57:* 5, pp. 706-708

LINDHOLM, T. : Anuri, post eller propter, hos obstetriska fall, behandlade med Ne-Hi-P-dropp (Anuria after or caused by obstetrical collapse treated with a nepresol-hibernal-pethidine preparation. Anurie à la suite de prostration obstétrique traitée au moyen d'une préparation nepresol-hibernal-péthidine). *Svenska Läkartidningen*, 1958, *55:* 22, pp. 1628-1630

LOUROS, N. & GOUSKOS, A. : Bemerkungen zur oxytozischen Wirkung des Dolantin (Oxytocic effect of Dolantin. Effet oxytocique de la dolantin). *Zeitschrift für Geburtshilfe und Gynäkologie*, 1958, *149:* 3, pp. 324-327

LYNCH, T. A. & MEYERS, D. B. : A study of the selective antagonism by N-allylnormorphine against meperidine, methadone and morphine. *Journal of the American Pharmaceutical Association, Sc. Ed.*, 1958, *47:* 5, pp. 323-325

M

MARGOLIUS, B. R. & KEPES, E. R. : Meperidine-levallorphan in anesthesia; study of usefulness of such mixtures in supplementation of nitrous oxide-oxygen-thiopental anesthesia. *American Journal of Surgery*, 1958, *95:* 5, pp. 787-792

MARKBY, C. E. : Intravenous pethidine in minor surgical procedures. *British Medical Journal*, 1958, No. 5084, pp. 1397

MAYKUT, M. O. : The combined action of pentobarbital and meperidine, and of procaine and meperidine, in guinea pigs. *Canadian Anaesthetists' Society Journal*, 1958, *5:* 2, pp. 161-169

MIGUEL MARTÍNEZ, J. : Pethidina. *Revista Española de Anestesiologia*, 1957, *4:* 3, pp. 209-221

MEGIRIAN, R. & WHITE Jr., C. W. : An evaluation of the respiratory and sedative effects of meperidine hydrochloride combined with levallorphan tartrate in postoperative patients. *New England Journal of Medicine*, 1957, *257:* 13, pp. 849-855

MORREN, H. & STRUBBE, H. : Analgésiques centraux. Dérivés de la 4-carbéthoxy-4-phényl-pipéridine. *Industrie chimique belge*, 1957, *22:* 7, pp. 795-798

P

PALIWODA, T. & ZIAREK, S. : Znaczenie pendiomidu i dolantyny we wstrząsie doświadczalnym (Significance of pendiomide and dolantin in experimental shock. Importance du pendiomide et de la dolantine dans le choc experimental). *Acta physiologica Polonica*, 1957, *8:* 4, pp. 655-660

PELTOLA, A. & SOISALO, P. : The analgesic properties and addiction liability of ketobemidone and morphine. *A.M.A. Archives of internal medicine*, 1958, *101:* 4, pp. 741-746

PERRINE, T. D. : Quinuclidines. I 4-Phenylquinuclidines as potential analgesics. *Journal of organic Chemistry*, 1957, *22:* 11, pp. 1484-1489

PORTER, C. C. : The absorption and metabolism of anileridine : ethyl-1-(4-amino-phenethyl)-4-phenylisonipecotate. *Journal of Pharmacology and Experimental Therapeutics*, 1957, *120:* 4, pp. 447-451

PORTOLANO, F.; CALIFANO, G. & DE FANIS, L. : Ricerche cliniche sul comportamento di alcuni indici della funzione surrenalica in rapporto alla preanestesia (Clinical research on the behaviour of various indices of adrenal function in relation to preanesthesia. Recherche clinique sur le comportement de divers indices de la fonction adrénale par rapport à la pré-anesthésie). *Rassegna Internazionale di Clinica e Terapia*, 1957, *37:* 20, pp. 936-941

R

RADOUCO-THOMAS, S.; RADOUCO-THOMAS, C. & LE BRETON, E. : Action de la noradrénaline et de la réserpine sur l'analgésie expérimentale. *N.-S. Archiv für experimentelle Pathologie und Pharmakologie*, 1957, *232:* 1, pp. 279-281

RIO, F. : Azione protettiva degli estratti lipoidei diencefalici sulle modificazioni indotte nei vari parenchimi dagli analgesici di sintesi. Ricerche sperimentali sul coniglio (Protective action of diencephalic lipoid extracts on changes induced in various parenchyma by synthetic analgesics. Experimental research on the rabbit. Action protectrice des extraits lipoïdiques diencéphaliques sur les modifications induites dans divers parenchymes par les analgésiques de synthèse. Recherches expérimentales sur le Lapin). *Endocrinologia e Scienza della costituzione*, 1957, *24:* 4, pp. 253-262

RODEN, J. S. & HAUGEN, H. M. : Evaluation of a new analgesic combination; report of use in postoperative gynecologic patients and in the postpartum period. *Missouri Medicine*, 1958, *55:* 2, pp. 128-129

RUZICSKA, J. & ZSOLNAI, B. : Résultats obtenus dans l'anesthésie gynécologique potentialisée. *Gynécologie et Obstétrique*, 1957, *56:* 3, pp. 287-294

SADOVE, M. S.; SCHIFFRIN, M. J.; NICKERSON, W. R. & GROVE, W. J : Use of meperidine and meperidine-levallorphan mixtures in the recovery room. *Journal of the American Medical Association*, 1958, *166:* 12, pp. 1432-1437

S

SCHIFFRIN, M. J.; BALAGOT, R. C. & SADOVE, M. S. : Some effects of levallorphan on responses to meperidine. *Canadian Anaesthetists' Society Journal*, 1957, *4:* 4, pp. 372-377

SMITH, C.; ROWE, R. D. & VLAD, P. : Sedation of children for cardiac catheterization with an ataractic mixture. *Canadian Anaesthetists' Society Journal*, 1958, *5:* 1, pp. 35-40

T

TOWNES, C. D. & MANN, S. H. : Intravenous sedation in cataract surgery. *American Journal of Ophtalmology*, 1958, *46:* 2, pp. 179-181

TRINCHÁN SÁNCHEZ, F. & NIETO AYESA, J. : Contribución a la farmacología

de la dolantina (The pharmacology of dolantin. Pharmacologie de la dolantine). *Archivos del Instituto de Farmacología experimental*, 1957, *9:* 1-2, pp. 193-201

U

UNGER, L. : Neue Wege in der konservativen Glaukomtherapie (New methods in the conservative treatment of glaucoma. Nouvelles méthodes dans la thérapie conservatrice du glaucome). *Medizinische Klinik*, 1957, *52:* 37, pp. 1629-1634

V

VANGELISTA, G.: Metilcolantrene ed etilchetone. Esperimenti e considerazioni sulla interferenza svolta dagli analgesici di sintesi sui tumori da idrocarburi cancerigeni : influenza del cloridrato di 1-metil-4 (metossifenil)-piperidin-4-etilchetone sulla insorgenza ed evoluzione dei tumori da 20-metilcolantrene nel ratto albino (Methylcholanthrene and ethylkefone experiments and considerations on interference with synthetic analgesics on malignant tumours due to carcinogenic hydrocarbons. Influence of 1-methyl-4 (metoxyphenyl) piperidine 4 ethylketone hydrochloride on starting and evolution of tumours caused by 20-methylcolanthrene in albino rats. Méthylcholanthrène et éthylcétone. Expériences et considérations sur des réactions d'interférence entre les analgésiques de synthèse et les tumeurs provoquées par les hydrocarbures cancérigènes : influence du chlorhydrate de méthyl-1 (métoxyphényl)-4, pipéridine-éthyl-4 cétone sur l'apparition et l'évolution des tumeurs dues au méthyl-20 cholanthrène chez le Rat blanc). *Neoplasie*, 1957, *10:* 2, pp. 113-123

VANGELISTA, G. & MAZZOLENI, G. : Interferenza alla insorgenza dell'arteriosclerosi sperimentale da adrenalina in conigli pretrattati con 1-metil-4 (m-ossifenil)-piperidin-4-etilchetone (Interference in the development of experimental arteriosclerosis due to adrenalin in rabbits pretreated with 1-methyl-4-(m-hydroxyphenyl)-4-propionyl-piperidine. Intervention dans le développement de l'artériosclérose expérimentale par l'anédraline chez le lapin traité auparavant avec la kétobémidone). *Endocrinologia e Scienza della Costituzione*, 1957, *23:* 6, pp. 411-419

VANGELISTA, G.; CAMERA, A. & DE GAETANI, G. : Modificazioni della costellazione neuroendocrina e dei vari parenchimi realizzate da dosi varianti di analgesici di sentesi : ricerche sperimentali con il cloridrato di 1-metil-4(m-ossifenil)-piperidin-4-etilchetone (cliradon) (Modifications of neuroendocrine constellations and of various parenchyma due to varied doses of synthetic analgesics; experimental research with 1-methyl-4-(m-hydroxyphenyl)-4-propionyl-piperidine. Modification des constellations neuro-endocrines et des différents parenchymes résultant de doses différentes d'analgésiques de synthèse. Recherches expérimentales sur le cliradon (Chlorhydrate de kétobémidone). *Ibid.*, *23:* 6, pp. 420-436

VASILYEVA, V. V.; LAKIN, K. M. & SERGEEV, P. V. : Effects of Promedol on the bioelectric activity of the cortex of the brain. *Bulletin on Narcotics*, 1958, *10:* 1, pp. 13-19; Influence du promédol sur l'activité bioélectrique du cortex cérébral. *Bulletin des stupéfiants*, 1958, *10:* 1, pp. 15-21

W

WALKENSTEIN, S. S.; MACMULLEN, J. A.; KNEBEL, C. & SEIFTER, J. : The metabolic fate of a hexamethylenimine analgesic. *Journal of the American Pharmaceutical Association, Sc. Edition*, 1958, *47:* 1, pp. 20-25

WEGRYN, S. P. & MARKS, R. A. : Promazine, meperidine, and spinal anesthesia for labor and delivery. *Journal of the American Medical Association*, 1958, *167:* 16, pp. 1918-1921

Z

ZIERING, A.; MOTCHANE, A. & LEE, J. : Piperidine derivatives. IV. 1,3-disubstituted-4-aryl-4-acyloxy piperidines. *Journal of Organic Chemistry*, 1957, *22:* 11, pp. 1521-1528

C. Methadone and related components — Méthadone et composés apparentés

A

ALMERSJO, O. : Palfium, ett nytt starkt analgetikum III. Prövning av Palfium vid radiumhemmet (Palfium, a new strong analgesic. III. Testing of palfium with radiotherapy. Palfium, nouvel analgésique puissant. III. Essai du palfium en radiothérapie). *Svenska läkartidningen*, 1958, *55:* 21, pp. 1531-1536

ANONYMOUS — ANONYME : Dextro-Propoxyphene hydrochloride. *Journal of the American Medical Association*, 1958, *166:* 12, pp. 1481-1482

B

BOUDIN, G. & BARBIZET, J. : Un analgésique central puissant : le R.875, le 2:2-diphényl-3 méthyl-4 morphine-butyryl-pyrrolidine base dextrogyre : son application en neurologie. *Presse médicale*, 1958, *66:* 7, pp. 131-134

BUCHEL, L.; LEVY, J. & TANGUY, O. : Sur la potentialisation de l'action analgésique de la 1-méthadone par la 5-hydroxytryptamine (sérotonine). *Comptes rendus hebdomadaires des séances de l'Académie des sciences*, 1958, *246:* 20, pp. 2947-2949

BUCHEL, L.; LEVY, J. & TANGUY, O. : Analogies structurales et synergie de l'action analgésique. III. Détermination, après un stimulus mécanique, de l'action analgésique d'associations d'analgésiques et de quelques types d'analogues structuraux doués de propriétés spasmolytiques. *Anesthésie, Analgésie, Réanimation*, 1957, *14:* 3, pp. 469-491

C

CAHAL, D. A. : Analgesic activity of (+)-1-(3-methyl-4-morpholino-2:2-diphenyl-butyryl) pyrrolidine (R.875) in student volunteers. *British Journal of Pharmacology and Chemotherapy*, 1958, *13:* 1, pp. 30-34

CAROLI, J. & CHARBONNIER, A. : A propos du traitement médical des pancréatites par le R.875; perspectives thérapeutiques nouvelles. *Revue médico-chirurgicale des maladies du foie, de la rate et du pancréas*, 1957, *32:* 3, pp. 41-54

CASTEL, P.; ATTISSO, M. & SERRE, L. : Quelques données sur un nouvel analgésique de synthèse à action centrale : Le R.875. *Travaux de la Société de Pharmacie de Montpellier*, 1957, *17:* 2, pp. 100-107

COCCHI, A. : R. 875 un nuevo analgésico heroico. (R.875 a new potent analgesic. R.875 un nouvel analgésique puissant). *Semana médica*, 1958, *112:* 14, pp. 497-507

COLEMEN, D. J.; HARGROVE, R. L. & JONES, P. O. : Controlled respiration by central depression. *Anaesthesia*, 1958, *13:* 1, pp. 59-62

D

DEMAILLY, M. L. : Le R.875 est un analgésique maniable, puissant et ne donnant pas d'accoutumance... *Gazette médicale de France*, 1958, *65:* 1, pp. 13-14

DE SÉZÉ, S.; CHEVALLIER, L. & TCHERDAKOFF : Experimentación clínica del nuevo analgésico R. 875 (Clinical experiments with the new analgesic R.875. Expérimentations cliniques avec le nouvel analgésique R.875). *Medicina Panamericana*, 1958, *10:* 7, pp. 221-226

DOUIN, J. : Toxicomanie au R.875 (2,2-diphényl-3 méthyl-4 morpholino-butyrylpyrrolidine dextrogyre). *Revue Médicale de Liège*, 1958, *13:* 10, pp. 332-333

F

FREE, S. M. & PEETERS, F. : Statistical comparison of methods to evaluate analgetics. *Journal of Chronic Diseases*, 1958, *7:* 5, pp. 379-384

FRIES, B. : Palfium, ett nytt starkt analgetikum. II. Palfium i kirurgisk praxis (Palfium, a new strong analgesic. II. Palfium in surgical practice. Palfium un nouvel analgésique puissant. II. Palfium en chirurgie). *Svenska Läkartidningen*, 1958, *55:* 20, pp. 1479-1484

J

JANSSEN, P. A. & JAGENEAU, A. H. : A new series of potent analgesics : dextro-2:2-diphenyl-3-methyl-4-morpholinobutyrylpyrrolidine and related basic amides. II. Comparatives analgesic activity, acute toxicity and tolerance development in rats for R.875, morphine, pethidine and methadone. *Journal of Pharmacy and Pharmacology*, 1958, *10:* 1, pp. 14-21

JONGH, D. K., DE & PROOSDIJ-HARTZEMA, E. G., van : Pharmacology of (+)-, (+)- and (—)-2:2-diphenyl-3-methyl-4-morpholinobutyrylpyrrolidine. *Journal of Pharmacy and Pharmacology*, 1957, *9:* 11, pp. 730-738

K

KEMPEN, H. G., van; PINCKAERS, J. A.; LOKIN, E. F. & HOLLEBEKE, F., van : Klinische ervaringen met een nieuw analge-

ticum (R.875, pyrrolamidolum) (Clinical experiences with a new analgesic (R.875, pyrrolamidolum). Expériences cliniques avec un nouvel analgésique (R.875, pyrrolamidolum)). *Nederlands Tijdschrift voor Geneeskunde*, 1958, *102:* 9, pp. 426-428

L

LA BARRE, J.; DESMAREZ, J. J. : Propriétés toxicomanogènes des dérivés des propylamines. L'expérimentation chez le Chien montre que, puisque l'assuétude des morphinisés se trouve abolie par un traitement approprié au R.875, il existe de fortes présomptions en faveur du caractère toxicomanogène de ce dérivé des propylamines. *Archives internationales de Pharmacodynamie et de Thérapie*, 1958, *114:* 3-4, pp. 480-481

LANGERON, L.; PAGET, M. & VINCENT, Jr., G. : Etude préliminaire sur les effets cliniques et biologiques du Palfium (R.875). *Journal des Sciences médicales de Lille*, 1958, *76:* 1, pp. 3-12

M

MENDES, F.; SANTOS, J. Dos & SOEIRO, N. : Primeiros casos de toxicomania pelo R.875 (First cases of toxicomania with R.875. Premiers cas de toxicomanie par le R.875). *Jornal do Médico*, 1958, *35:* 792, pp. 761-762; passim

N

NORDVALL, S. : Palfium, ett nytt starkt analgetikum. IV. Palfium i obstetrisk praxis (Palfium, a new strong analgesic. IV. Palfium in obstetrical practice. Palfium, nouvel analgésique puissant. IV. Palfium en obstétrique). *Svenska Läkartidningen*, 1958, *55:* 21, pp. 1536-1538

P

PEDRAZZOLI, A.; ROGGERO, M. : Nuovi farmaci 1957 (New remedies 1957. Nouveaux médicaments 1957). *Bollettino chimico farmaceutico*, 1958, *97:* 4, pp. 213-228

PEETERS, F. : Etude clinique de l'emploi du R.875 en obstétrique. *Presse médicale*, 1958, *66:* 1, pp. 8-9

PROKOP, H. & JOST, F. : Ticardasucht (Ticarda addiction. Toxicomanie à la Ticarda). *Wiener klinische Wochenschrift*, 1958, *70:* 10, pp. 172-175

PROOSDIJ-HARTZEMA, E. G. Van, & JONGH, D. K. de : A series of potent analgesics. *Acta physiologica et pharmacologica neerlandica*, 1957, *5:* 4, pp. 398-405

R

RICCI, G. & JACOVELLA, G. : Un nuovo potente analgesico di sintesi; l'R.875 (A powerful new synthetic analgesic, R.875. Un puissant nouvel analgésique de synthèse, le R.875). *Clinica terapeutica*, 1958, *14:* 6, pp. 649-655

RIVERA LÓPEZ, R. : Grave accidente respiratorio por empleo del antiálgico R.875 (Severe respiratory accident caused from the use of analgesic R.875. Grave accident respiratoire dû à l'emploi de l'analgésique R.875). *Revista Clínica Española*, 1958, *68:* 6, pp. 380-381

ROCHE, L.; BETHENOD, M & TOMMASI, M : Un cas de mort par absorption de R.875 (Palfium). *Annales de médecine légale et de criminologie*, 1958, *38:* 6, pp. 375-378

ROSE, H. A. : A note on the crystallography of d-propoxyphene hydrochloride. *Journal of the American Pharmaceutical Association*, Sc. ed., 1958, *47:* 3, Pt. I, p. 228

ROVATI, L. : Un nuovo analgesico di sintesi : R.875 (A new synthetic analgesic : R. 875. Un nouvel analgésique de synthèse : le R.875). *Farmaco ed. pract.*, 1958, *13:* 4, pp. 186-194

S

SANDBERG, F. : Palfium, ett nytt starkt analgetikum. I. Farmakologi (Palfium, a new strong analgesic. I. Pharmacology. Palfium, un nouvel analgésique puissant. I. Pharmacologie). *Svenska Läkartidningen*, 1958, *55:* 20, pp. 1474-1479

SERRE, L.; ATTISSO, M.; TEMPLE, J. P. & SARTRE, M. : Premiers résultats de l'expérimentation clinique du R.875 au Centre Hospitalier Régional de Montpellier. *Anesthésie, Analgésie, Réanimation*, 1958, *15:* 1, pp. 97-105

SLAVIERO, E. : " R.875 " : Recente analgesico di sintesi (Recent synthetic analgesic. Récent analgésique de synthèse). *Bollettino Chimico farmaceutico*, 1958, *97:* 4, pp. 229-233

SOUPAULT, R.; CAROLI, J.; RENON, M.; SCHOPS, T. & CHARBONNIER, A. : Premiers essais en clinique humaine d'un nouvel analgésique de synthèse : le 2-2 diphényl-3-méthyl-4-morpholino-buturyl-pyrrolidine base dextrogyre (R.875). *Thérapie*, 1957, *12:* 6, pp. 898-910

SOUPAULT, R. & CAROLI, J. : Estudio clinico del nuevo analgésico sintético R.875 (Clinical study of the new synthetic analgesic R.875. Etude clinique du nouvel analgésique de synthèse R.875). *Día médico*, 1958, *30:* 17, p. 533; passim

STARACE, G. & NOFERI, A. : L'R.875 (Palfium) quale preanestetico in broncologia (R.875 (Palfium) as pre-anaesthetic in bronchology. Le R.875 (Palfium) comme preanesthétique en bronchologie). *Minerva medica*, 1958, *49:* 11, pp. 422-424

T

TEMPLE, J. P.; ATTISSO, M. & SERRE, L. : A propos d'un traitement de toxicomanie eubinique par le R.875. *Travaux de la Société de Pharmacie de Montpellier*, 1957, *17:* 3, pp. 130-133

D. Morphinan and morphine synthesis — Morphinane et synthèse de la morphine

E

EDDY, N. B.; BESENDORFF, H. & PELLMONT, B. : Synthetic analgesics. IV. Aralkyl substitution on nitrogen of morphinan. *Bulletin on Narcotics*, 1958, *10:* 4, pp. 23-41; Analgésiques de synthèse. IV. Substitution arylalcoylée sur l'azote du morphinane. *Bulletin des stupéfiants*, 1958, *10:* 4, pp. 25-44

EDDY, N. B.; MURPHY, J. G. & MAY, E. L. : Structures related to morphine. IX. Extension of the Grewe morphinan synthesis in the benzomorphan series and pharmacology of some benzomorphans. *Journal of Organic Chemistry*, 1957, *22:* 11, pp. 1370-1372

G

GANGLOFF, H.; MONNIER, M. : The topical action of morphine, levorphanol (levorphan) and the morphine antagonist levallorphan on the unanaesthetized rabbit's brain. *Journal of Pharmacology and experimental Therapeutics*, 1957, *121:* 1, pp. 78-95

GARANT, O.; SAINT-ARNAUD, G. & CAOUETTE, M. : Le lorphan en obstétrique. *Laval Medical*, 1958, *25:* 1, pp. 31-40

GATES, M. & WEBB, W. G. : The synthesis and resolution of 3-hydroxy-N-methylisomorphinan. *Journal of the American Chemical Society*, 1958, *80:* 5, pp. 1186-1194

GRIESSER, G. : Ueber die Hemmung der Antidiuretischen Wirkung von Morphin und Dromoran durch (——)-3-Hydroxy-N-allyl-Morphinan (Laevallorphan) beim Menschen (Inhibition in man of antidiuretic action of morphine and of Dromoran by means of (—) 3-hydroxy-N-allylmorphinane. Sur l'inhibition chez l'Homme, de l'action antidiurétique de la morphine et du Dromoran par le (—) hydroxy-3-N-allyl-morphinane (Lévallorphan). *Klinische Wochenschrift*, 1957, *35:* 17, pp. 851-855

GRUHZIT, C. C. : Chemoreflex activity of dextromethorphan (romilar), dextrorphan, codeine and morphine in the cat and the dog. *Journal of Pharmacology and experimental Therapeutics*, 1957, *120:* 4, pp. 399-407

H

* HARASAWA, K. : (Syntheses of quinoleic analogues of N-methylmorphinane. Synthèses d'analogues quinoléiques du N-méthylmorphinane). *Journal of the Pharmaceutical Society of Japan*, 1957, *77:* 2, pp. 168-172

* HARASAWA, K. : (Resolution of optically active N-methyl-15-aze-des-N-morphinane and of its Hydroxy derivatives. Résolution du N-méthylaza-15 des -N-morphinane optiquement actif et de ses dérivés hydroxy). *Journal of the Pharmaceutical Society of Japan*, 1957, *77:* 2, pp. 172-174

HUNTER, A. R. : Levallorphan in anaesthesia. *British Journal of Anaesthesia*, 1958, *30:* 5, pp. 233-239

M

MAY, E. L. & FRY, E. M. : Structures related to morphine. VIII. Further syntheses in the benzomorphan series. *Journal of Organic Chemistry*, 1957, *22:* 11, pp. 1366-1369

MAY, G.; PHILLIPS, M. & ADRIANI, J. : Effect of N-allylnormorphine and levallorphan

on respiration during and after ether anesthesia. *Anesthesiology*, 1957, *18:* 6, pp. 871-877

S

SUGIMOTO, N. & OHSHIRO, S. : Studies on the syntheses of hydrogenated quinolines and isoquinolines as analgesics. XIII. Synthesis of 3-hydroxy-N-methyl-6-aza-des-N-morphinan (N-methyl-9-hydroxy-5, 10 b-tri-methylene-1, 2, 3, 4*a*, 5, 6, 10*b*-octahydrobenzo (h) isoquinoline). *Pharmaceutical Bulletin*, 1957, *5:* 4, pp. 316-319

SUGIMOTO, N. & KUGITA, H. : Studies on the syntheses of hydrogenated quinolines and isoquinolines as analgesics. XIV. Synthesis of 6-hydroxy-4a, 10-trimethylene-1, 2, 3, 4, 4a, 9, 10, 10a-octahydrophenanthridine (Supplement). *Pharmaceutical Bulletin*, 1957, *5:* 4, pp. 378-380

SWERDLOW, M. : Levallorphan; effects of large doses. *Anaesthesia*, 1958, *13:* 3, pp. 318-323

T

TABORSKY, L. : Ueber die Behandlung einer Pantoponvergiftung mit dem Morphinantagonisten Allylderivat Ro 1-7700 (Treatment of pantopon pisoning with a morphine antagonist allylderivative, Ro 1-7700. Traitement d'un empoisonnement au pantopon par un dérivé allylique et antagoniste de la morphine, Ro 1-7700). *Wiener medizinische Wochenschrift*, 1958, *108:* 10, pp. 220-221

TAKEMORI, A. E. & MANNERING, G. J. : Metabolic N- and O-demethylation of morphine- and morphinan-type analgesics. *Journal of Pharmacology and experimental Therapeutics*, 1958, *123:* 3, pp. 171-179

TAYLOR, H. E.; DOERR, J. C.; GHARIB, A. & FAULCONER, Jr. A., : Effect of preanesthetic medication of ether content of arterial blood required for surgical anesthesia. *Anesthesiology*, 1957, *18:* 6, part I, pp. 849-855

Part VI. — ADDICTION TO NARCOTIC DRUGS — TOXICOMANIE

A

ALTER, A. A. & MICHAEL, Jr., M. : Serum hepatitis in a group of drug addicts. *New England Journal of Medicine*, 1958, *259:* 8, pp. 387-389

A.M.A. Council on Mental Health : Report on narcotic addiction. *Journal of the American Medical Association*, 1957, *165:* 13, pp. 1707-1713; 14, pp. 1834-1841; 15, pp. 1968-1974

ANGELUCCI, L. : Influenza della somministrazione di cocarbossilasi sulla assuefazione alla morfina nel ratto (Effect of the administration of cocarboxylose on morphine habituation in the rat. Influence de l'administration de cocarboxylase sur l'accoutumance à la morphine chez le Rat). *Bollettino della Società italiana di Biologia sperimentale*, 1957, *33:* 10-11, pp. 1403-1406

ANONYMOUS — ANONYME : Chasing the dragon (The smoking of heroin in Hong Kong). *Bulletin on Narcotics*, 1958, *10:* 3, pp. 6-7; " La chasse au dragon " (Les fumeurs d'héroïne à Hong Kong). *Bulletin des stupéfiants*, 1958, *10:* 3, pp. 6-7

ANONYME : L'ONU et la toxicomanie. *Santé publique*, 25 février 1955, No. 96

AXELROD, J. : Possible mechanism of tolerance to narcotic drugs. *Science*, 1956, *124:* pp. 263-264

B

BATTEGAY, R. : Individuelle und soziale Ursachen, Prognose und Prophylaxie der Sucht mit Analgetica (Individual and social cause, prognosis and prophylaxis of analgesic addiction. Causes individuelles et sociales, prognostic et prophylaxie de la toxicomanie aux analgésiques). *Schweizerische medizinische Wochenschrift*, 1958, *88:* 4, pp. 89-92

BERGER, H. : Narcotics addiction among physicians. *Postgraduate medicine*, 1958, *23:* 1, pp. 100-102

BILLIG, O. & BURRIS, B. L. : Habituation to tranquillizing drugs. *Journal of the Tennessee State Medical Association*, 1957, *50:* 10, pp. 406-407

BRUNNER-ORNE, M. : The utilization of group psychotherapy in enforced treatment programs for alcoholics and addicts. *International Journal of Group Psychotherapy*, 1956, *6*, pp. 272-279

C

CALLAWAY, E. : The abuse of narcotics by patients suffering from cancer. *Journal of the Medical Association of Georgia*, 1958, *47:* 7, p. 355

CAMP, W. J. : Drivers, drinks and drugs. *Postgraduate Medicine*, 1957, *22:* 1, pp. A-38 passim

CAVELL, R. W. : Aspects of narcotic addiction. *University of Michigan Medical Bulletin*, 1957, *23:* 12, pp. 458-463

CHAPMAN, K. W. : Care and treatment of drug addicts. *Bulletin on Narcotics*, 1958, *10:* 2, pp. 25-28; Traitement médical et social des toxicomanes. *Bulletin des stupéfiants*, 1958, *10:* 2, pp. 25-29

COTLAR, N. : Coma and psychosis following possible insulin hypersensitivity; with remission of narcotic addiction after severe hypoglycemic shock. *Texas State Journal of Medicine*, 1957, *53:* 11, pp. 860-862

COURTNEY, C. F. : 100 years ago : an essay on opium smoking. *Journal of the Royal Naval Medical Service*, 1957, *43:* 3, pp. 147-152

CRIKELAIR, G. F. : Drug addiction in reconstructive surgery. *Plastic and Reconstructive Surgery*, 1957, *19:* 5, pp. 424-430

D

DANNER, H. : Prevention of narcotic offences. *Bulletin on Narcotics*, 1958, *10:* 2, pp. 35-37; Prévention des délits dus à la toxicomanie. *Bulletin des stupéfiants*, 1958, *10:* 2, pp. 36-38

DAVIDIAN, H. : The treatment of withdrawal symptoms of opium addicts with vitamin E in ten cases. *Acta Medica Iranica*, 1957, *1:* 3, pp. 215-221

DENEAU, G. A. : An analysis of the factors influencing the development of physical dependence to narcotic analgesics in the rhesus monkey with methods for predicting physical dependence liability in man. *Dissertation Abstracts*, 1958, *18:* 4, pp. 1455-1456

DIAMOND, M. D. : Role-taking ability and schizophrenia. *Journal of Clinical Psychology*, 1958, *14:* 3, pp. 321-324

F

FIERZ, H. K. : Delirium tremens bei Schlafmittelsucht (Delirium tremens in hypnotic addiction). *Schweizerische Medizinische Wochenschrift*, 1958, *87:* 34, pp. 1098-1099

FOLTZ, E. L. & WHITE Jr., L. E., : Experimental cingulumotomy and modification of morphine withdrawal. *Journal of Neurosurgery*, 1957, *14:* 6, pp. 655-670; discussion, pp. 670-673

FRASER, H. F.; WIKLER, A.; ESSIG, C. F. & ISBELL, H. : Degree of physical dependence induced by secobarbital or pentobarbital. *Journal of the American Medical Association*, 1958, *166:* 2, pp. 126-129

FRASER, H. F.; WIKLER, A.; VAN HORN, G. D.; EISENMANN, A. J. & ISBELL, H. : Human pharmacology and addiction liability of normorphine. *Journal of Pharmacology and Experimental Therapeutics*, 1958, *122:* 3, pp. 359-369

FUJIMOTO, J. M. & WAY, E. L. : Isolation and crystallization of bound morphine from urine of human addict. *Journal of Pharmacology and experimental Therapeutics*, 1957, *121:* 3, pp. 340-346

G

GLASPEL, C. J. : Problems in narcotic addiction. *Federation Bulletin*, 1958, *45:* 7, pp. 200-207

GOSSELIN, J. Y.; JOHNSON G. & TURMEL, J. : Chlorpromazine et sevrage brusque de toxicomanes. *Laval Médical*, 1958, *26:* 1, pp. 28-33

GUILLOT, M. : Evolution de la notion de toxicité des médicaments. *Bollettino chimico farmaceutico*, 1958, *97:* 5, pp. 289-306

H

HERKEN, H. : Die Gewöhnung an Arzneimittel (Habituation. Accoutumance). *Aerztliche-Wochenschrift*, 1957, *12:* 50, pp. 1117-1123

HOYER, H. : Wider die Allmacht der Tabletten (Protest against the omnipotence of tablets. Contre la toute-puissance des comprimés). *Hippokrates*, 1958, *29:* 6, p. 187

HORMIA, A. : Psychose épileptique caractérisée par une panique homosexuelle dans la phase

d'abstinence consécutive à un barbiturisme chronique; exemple de concours de facteurs psychogènes et somatiques. *Encéphale*, 1957, *46:* 3, pp. 245-252

HUBBLE, D. : Opium addiction and English literature. *Medical History*, 1957, *1:* 4, pp. 323-335

J

JONES, L. E. : Experience with probation in California. *Federation Bulletin*, 1958, *45:* 6, pp. 165-173

K

KOON, L. Hon : The opium problem in Singapore. *Bulletin on Narcotics*, *10:* 4, pp. 7-11; Le problème de l'opium à Singapour. *Bulletin des stupéfiants*, *10:* 4, pp. 7-12

KOSTER, S. : Pijn, slapeloosheid, geneesmiddelenverslaving en hypnose (Pain, sleeplessness, drug addiction and hypnosis. Douleur, insomnie, toxicomanie et hypnose). *Geneeskundige Gids*, 1958, *36:* 7, pp. 109-113

KRAUSE, S. O.; MURRAY, P. M.; HOLMES, J. B. & BURCH, R. E. : Heroin addiction among pregnant women and their newborn babies. *American Journal of Obstetrics and Gynecology*, 1958, *75:* 4, pp. 754-758

KUSHNER, D. S. & SZANTO, P. B. : Heart failure, fever and splenomegaly in a morphine addict. *Journal of the American Medical Association*, 1958, *166:* 17, pp. 2162-2167

L

LANDAU, R. : Medical management of acute withdrawal symptoms in juvenile male and female heroin addicts; a preliminary report. *Illinois Medical Journal*, 1958, *113:* 1, pp. 13-15

LAUBENTHAL, F. : Zur Psychologie und Pathogenese der Suchterscheinungen (Psychology and pathogenesis of addiction. Psychologie et pathogenèse de la toxicomanie). *Deutsches medizinisches Journal*, 1957, *8:* 12, pp. 587-593

LOWRY, J. V. : Treatment of the drug addict at the Lexington (Ky.) hospital. *Bulletin on Narcotics*, 1958, *10:* 1, pp. 9-12; Le traitement des toxicomanes à l'hôpital de Lexington (Kentucky). *Bulletin des stupéfiants*, 1958, *10:* 1, pp. 10-14

M

McMAHON, J. E. : Notes on the treatment of opium addiction. *Medical Journal of Malaya*, 1957, *12:* 1, pp. 373-378

MALLER, O. & CONSTANTINESCU, G. N.: Rauschgiftsucht infolge Hustenlinderungsmittel (Narcotic drug addiction due to the use of anti-cough drugs. Toxicomanie par l'emploi d'antitussifs). *Psychiatrie, Neurologie und medizinische Psychologie*, 1958, *10:* 2, pp. 53-57

MARRUBINI, G. & BERNARDI, L. : Il tema di imputabilità dei tossicomani (The responsibility of drug addicts. Les toxicomanes sont-ils responsables?) *Rivista sperimentale di Frenatria e Medizina legale delle Alienazioni mentali*, 1957, *81:* 3, pp. 777-786

MEERLOO, J. A. : Variable individual tolerance for alcohol and drugs; some dangerous social implications. *Postgraduate medicine*, 1957, *22:* 6, pp. 583-590

MERCIER, J.; ETZENSPERGER, P. & CHATAIN, R. A. : Peut-on utiliser la souris pour déterminer l'accoutumance par la méthode de la tolérance aux doses toxiques? *Annales pharmaceutiques françaises*, 1957, *15:* 12, pp. 701-712

MONROE, J. J. & HILL, H. E. : The Hill-Monroe inventory for predicting acceptability for psychotherapy in the institutionalized narcotic addict. *Journal of Clinical Pathology*, 1958, *14:* 1, pp. 31-36

O

O'DRISCOLL, W. G. & LINDLEY, G. R. : Self-administration of tripelennamine by a narcotic addict. *New England Journal of Medicine*, 1957, *257:* 8, pp. 376-377

OSBERG, J. W. & BERLINER, A. : The development stages in group psychotherapy with hospitalized narcotic addicts. *International Journal of Group Psychotherapy*, 1956, *6*, pp. 436-446

P

PLICHET, A. : Problèmes de la toxicomanie chez les jeunes et l'évolution de la civilisation. *Presse médicale*, 1955, supplément au N° 67, pp. 365-366

R

RADO, S. : Narcotic bondage. *American Journal of Psychiatry*, 1957, *114*, pp. 165-170

REMMER, H. & ALSLEBEN, B. : Die Aktivierung der Entgiftung in den Lebermikrosomen während der Gewöhnung (Activation of detoxication in liver microsome during addiction. Activation de la détoxication dans le microsome hépathique au cours de la toxicomanie). *Klinische Wochenschrift*, 1958, *36:* 7, pp. 332-333

ROMAN, L. P. & MIDDELKAMP, J. N. : Narcotic addiction in a newborn infant. *Journal of Pediatrics*, 1958, *53:* 2, pp. 231-232

RUSSO, A. J. : Observations on narcotic addicts having about 200 habit years. *American Practitioner and Digest of Treatment*, 1958, *9:* 4, pp. 603-606

S

SAINZ, A. A. : The treatment of drug and alcohol-withdrawal effects with thorazine. *Psychiatric Quarterly*, 1957, *31:* 2, pp. 275-284

SAUTER, A. : Der Analgeticamissbrauch als Problem des öffentlichen Gesundheitswesens (Abuse of analgesics as a social hygiene problem. L'abus des analgésiques en tant que problème d'hygiène sociale). *Bulletin der Schweizerischen Akademie der medizinischen Wissenschaften*, 1958, *14:* 2, pp. 93-99

SCHMID, H. J. : Die moderne Schmerzmittel-Süchtigkeit (Present-day analgesic addiction. La toxicomanie moderne aux analgésiques). *Veska-Zeitschrift*, 1958, *22:* 2, pp. 63-67

SCHNECK, H. : Narcotic withdrawal symptoms in the newborn infant resulting from maternal addiction. *Journal of Pediatrics*, 1958, *52:* 5, pp. 584-587

STEG, N. : Narcotic withdrawal reactions in the newborn. *Journal of Diseases of Children*, 1957, *94:* 3, pp. 286-288

SZASZ, T. S. : The role of the counterphobic mechanism in addiction. *Journal of the American Psychoanalytic Association*, 1958, *6:* 2, pp. 309-325

T

TAKMAN, J. : Om narkotikamisbruk bland ungdom (Drug addiction among Stockholm's youth. Toxicomanie parmi la jeunesse de Stockholm). *Sociala meddelanden*, 1958, No. 1, pp. 25-32

TOLENTINO, I. : Considerazioni psicopatologiche su due casi di tossicomania e psicosi da derivati fenilpropilaminici (Psychopathological and clinical findings in two cases of addiction to and psychoses caused by phenylpropylamine derivatives. Conclusions psychopathologiques et cliniques dans deux cas de toxicomanie et psychoses causés par les dérivés phénylpropylaminiques). *Rivista di Neurologia*, 1958, *28:* 1, pp. 81-90

TON-THAT-TUNG : Chirurgie der Opiumsüchtigen (Surgery in opium addicts. Les opiomanes en chirurgie). *Zentralblatt für Chirurgie*, 1957, *82:* 31, pp. 1305-1309

V

VAILLE, Ch. : *La réglementation des substances vénéneuses; les toxicomanies*. Ed. du Creuset 1957, Paris. 356 pp.

VARENNE, G. : Quelques aspects du problème des stupéfiants et de la toxicomanie, principalement en Belgique. *Revue de droit pénal et de criminologie*, 1958, *38*, pp. 805-826

W

WHO : Treatment and care of drug addicts : Report of a study group. *WHO Technical Report Series*, 1957, No. *131*, pp. 3-19

WILLIAMS, Jr., G. H. : Drug Addiction. *Pennsylvania Medical Journal*, 1957, *60:* 11, pp. 1441-1446

WALL, J. H. : The results of hospital treatment of addiction in physicians. *Federation Bulletin*, 1958, *45:* 5, pp. 144-152

* WONG, T. P. : (Manual on the prevention of opium addiction [in Chinese]. Prévention de l'opiomanie : Manuel [en chinois]).

Y

YAO, Y. L. : The single Convention on narcotic drugs and the prevention of drug addiction. *Bulletin on Narcotics*, 1958, *10:* 1, pp. 1-8; La Convention unique sur les stupéfiants et la lutte contre la toxicomanie. *Bulletin des stupéfiants*, 1958, *10:* 1, pp. 1-9

YAO, Y. L. : How to combat drug addiction : the Chinese experience. *Bulletin on Narcotics*, 1958, *10:* 4, pp. 1-6; Comment lutter contre la toxicomanie. *Bulletin des stupéfiants*, 1958, *10:* 4, pp. 1-6

Part VII. — MISCELLANEOUS — DIVERS

A

AKIYA, S.; NAKAZAWA, Y. & ISHIKURA, S. : En japonais (Detection of dilkylamino-dithienyl butane. Détection du dialkylamino-dithiénylbutène). *Journal of the pharmaceutical Society of Japan*, 1957, *77:* 8, pp. 931-933

ANON : Un stupéfiant mal connu, le cath " catha edulis ". *Revue internationale de police criminelle*, 1958, *13:* 116, pp. 85-88

B

BEASLEY, Y. M.; PETROW, V. & STEPHENSON, O. : Analgesics. I. Some aryloxy-propanolamines. *Journal of Pharmacy and Pharmacology*, 1958, *10:* 1, pp. 47-59

G

GROSS, F. & TURRIAN, H. : Ueber Benzimidazolderivate mit starker analgetischer Wirkung (Strong analgesic action benzimidazol derivatives. Dérivés du benzimidazole à action analgésique marquée). *Experientia*, 1957, *13:* 10, pp. 401-402

M

MANNING, J. J. & O'BRIEN, K. P. : The analysis of barbiturates by the pressed bromide sampling method and infra-red spectrophotometry. *Bulletin on Narcotics*, 1958, *10:* 1, pp. 25-34; Analyse des barbituriques par la méthode de l'échantillon dans le disque de bromure comprimé et la spectrophotométrie infrarouge. *Bulletin des stupéfiants*, 1958, *10:* pp. 27-37

P

PARIS, R. & MOYSE, H. (Mme) : Essai de caractérisation du kat ou thé des abyssins. *Annales pharmaceutiques françaises*, 1957, *15:* 2, pp. 89-97

PARIS, R. & MOYSE, H. (Mme) : Abyssinian tea. *Bulletin on Narcotics*, 1958, *10:* 2, pp. 29-34; Le thé des Abyssins. *Bulletin des stupéfiants*, 1958, *10:* 2, pp. 30-35

S

SLOTKIN, J. S. : The peyote religion. A study in Indian-White relations. 1956. *Free Press*, Glengo, Ill. (U.S.A.), 195 pp. plus vii. ill. bibliogr.

ERRATUM

Vol. XI, No. 1

In table of contents, title of second article should read: " The rate of development of physical dependence and tolerance to analgesic drugs in patients with chronic pain. I. Comparison of morphine, oxymorphone and anileridine "

p. 3. In title, insert " I. " before " Comparison of morphine," etc.

p. 4. Footnote (*), delete: " through the courtesy of Dr. M. J. Lewenstein ".

p. 6. Left-hand column, 10 lines from bottom, insert " almost " before always.

p. 5. Table 2, in " 1st day " column, opposite " A.S. ", " 1 × 1.35 " should read " 1 × 0.35 ".

p. 7. Table 4, last line in column " 2 ", instead of " 16.6 ", read " 16.4 ".

p. 8. Table 5, " 6-week " column, delete " (2) " on top line. Insert " (2) " in last column. At bottom of table, opposite " Average ",
instead of " 0.63 " read " 0.60 "
instead of " 0.81 " read " 0.79 "
instead of " 20.18 " read " 20.08 "
— —
— —
instead of " 26.55 " read " 27.22 "
Opposite " Average *** ", instead of " 0.66 " read " 0.67 "
— —
instead of " 21.85 " read " 21.59 "
— —
— —
instead of " 26.55 " read " 27.22 "
Opposite " Percentage increase ", instead of " 22.7 " read " 20.9 "
instead of " 28.6 " read " 31 "
instead of " 21.5 " read " 26.0 "

p. 9. Table 6, opposite " Average *** ", in the " 3-week " column, instead of "28.86" read "24.99".
opposite "Percentage increase" in the "1-week" column, delete "62.9"
Table 7, opposite " Average ", in the " 1-week " column, instead of " 15.66 " read " 15.73 "
opposite " Average *** ", in 1st column, instead of " 0.57 " read " 0.53 "
opposite " % increase " in 2nd column, instead of " 43.9 " read " 54.7 "
opposite " % increase " in 3rd column, instead of " 46.6 " read " 46.5 "
opposite " % increase " in 7th column, instead of " 54.9 " read " 54.3 "

p. 15. Table 13, last column, top line, " 5/4" should be " 5.4 ".

UNITED NATIONS

PUBLICATIONS ON NARCOTIC DRUGS

Commission on Narcotic Drugs. REPORT OF THE THIRTEENTH SESSION, 28 APRIL - 30 MAY 1958, ECONOMIC AND SOCIAL COUNCIL, OFFICIAL RECORDS, TWENTY-SIXTH SESSION, SUPPLEMENT No. 9. English, French and Spanish editions published annually. . . . . *Price per issue:* $0.80; 5/6 stg. Sw. Fr. 3.50

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